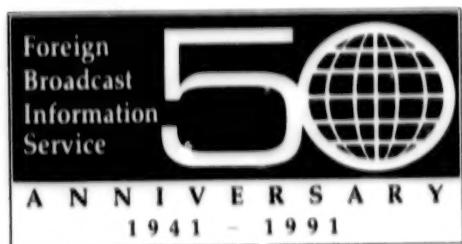


JPRS-ULS-91-006  
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# ***JPRS Report***

## **Science & Technology**

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***USSR: Life Sciences***

# Science & Technology

## USSR: Life Sciences

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### Habitability and Biological Life Support Systems

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[Article by O. G. Gazeiko, A. I. Grigoryev, G. I. Meleshko, and Ye. Ya. Shepelev]

[Text] The authors see the merit of discussing the problems posed in this article about man's attitude toward biological life support systems (BLSS) and his understanding of their purpose and role in the future of cosmonautics depend on an understanding of the problem of habitability. If we base the concept of habitability on the satisfaction of a familiar list of individual physiological and hygiene requirements, then we can understand the task of life support systems purely as consumers—as one of ensuring the parameters required of the environment and the amount of its required components—oxygen, water, and food. If we base the problem on the ecological concept of the habitat in the broad sense, then ecological, not consumer, requirements must be imposed on the LSS as a system for total development of a biologically complete habitat adequate for man's biological needs and meeting, in principle, the basic criteria of the natural environment on Earth.

This is the reason for the different approaches to evaluating the prospects of BLSS used by designers on the one hand and doctors studying human living conditions in space facilities on the other.

The importance of "defining relations" between the concept of habitability and the role of the means that ensure it is especially great in the discussion of programs imminent for cosmonautics, such as the lunar base or flight to Mars, which require man's prolonged separation from direct contact with the Earth's biosphere. Under these conditions the role of the concept of habitability and, therefore, of the life support system becomes decisive in ensuring the reliability of the programs themselves. Then the understanding of a BLSS as a closed ecological system, as a certain extension of the terrestrial biosphere, will be more adequate to the concept of habitability for many years of extraterrestrial human activity.

Prospects for more prolonged self-contained human existence outside the biosphere are related to the transition from a habitat natural for terrestrial organisms to an artificial environment that is entirely different in origin and quality and created from scratch by man by regenerating it from products of vital activity. This raises the question of reconsidering the concept of habitability for its new application.

The published literature does not contain a complete and final explication of the current concept, nor is there an unambiguous definition of the term "habitability". This situation has been successfully reflected by Yu. A. Petrov

in a joint Soviet-American collaboration [16]. In the chapter "Physiological, Hygienic, and Psychological Aspects of Life in a Spacecraft Cabin", he writes, "The range of problems covered is difficult to join into a single whole without turning to the complicated concept of habitability, which has not been delimited clearly enough." American authors also point out the indeterminacy of the concept of habitability [22, 23]. T. Fraser [24] defines habitability as the quality of environmental conditions evaluated in terms of their suitability for man. The idea contained in this definition, that man is himself the criterion, the measure of habitability imposes itself too much. The latest definition of this concept in our literature is interpreted as a "set of ecological and hygiene conditions created as a result of man's vital activity in a sealed cabin through the use of a life-support system" [10]. This definition is unacceptable from our standpoint because it makes the content of a certain concept dependent on specific LSS.

The latest edition of our professional reference [15] defines habitability as "the totality of ecological and hygiene factors to which man can adapt while retaining his health and high level of job performance." The Large Medical Encyclopedia contains an article on "habitability" that also considers possibilities for human adaptation [14]. From our standpoint the definition should not contain the component of adaptation. We can hardly permit any consumption of the body's adaptive reserves even in the initial period of existence in a self-contained facility.

We think that habitability can be defined as the totality of environmental conditions (physical, chemical, biological, and social) which ensure the environment's suitability for normal human vital activity without time limit or for a stipulated period (limited habitability). Obviously, at this stage, we are still concerned with the limited habitability of space facilities. Given this definition, the future goal of human space ecology is clear—reducing limits on habitation time (of course, not at the expense of man) and turning the limited habitability of space facilities into unlimited. As regards the practical ways to support space flights in the foreseeable future, they will, to a significant extent, be related to solving the problem of how inadequate the artificial environment in space facilities can be in terms of the natural terrestrial habitat.

Concerning notions of habitability on extended space flights, historically there were doubts, at first, about the level and constancy of calculated atmospheric parameters. The fact is that, despite the lack of an explicit concept of habitability, its basic tenets can be seen in actual space medicine practice. For example, the practice of standardizing the habitat in spacecraft and stations in terms of microclimate parameters, atmospheric pressure, and gas composition is clearly based on the requirements of physiological and hygienic comfort.

Twenty-five years ago, A. M. Genin [6] was the first in our literature and, apparently, in world literature to

point out that the concept of a comfortable or "neutral" environment was unacceptable for long flights. He raised the question of using fluctuations in certain atmospheric parameters to actively stimulate the human body, as well as the more general problem of the environment's active role in supporting the body's significant regulatory reserves. Then certain other problems of human ecology were raised, including those applying to human BLSS conditions [7, 21].

This first attempt at a new approach to the problem of spacecraft habitability was later continued [4, 5]. These works developed the notion of the biological completeness of a BLSS habitat biogenic in its origin by analogy with the natural environment, while they attributed the idea of the active influence of the environment to specific physiological mechanisms of respiration, temperature regulation, and circulation, which is related to them. Of course, when flights were measured in weeks, these considerations were too premature and did not attract attention. But now, in foreseeing Martian programs, we should return to them and try to analyze the possibility of using them in a new concept of habitability.

But this is only one, and not the main, aspect of habitability, although the dynamic characteristics of the environment's physical parameters and gas composition are of great physiological significance. The basic content of the habitability problem—the quality of living conditions—pertains to the entire set of environmental factors that make an environment suitable for life.

Our current knowledge of man's habitat is the traditional sphere of the set of physiological and hygiene disciplines which study and standardize the factors that are most significant for man, air, water, and food products. Somehow, possibly unconsciously but justifiably, we assume that everything outside the framework of hygienic standardization is somehow automatically provided *a priori* by the complete natural environment—the natural atmosphere, natural water, natural food, animals and plants. This ambiguous logic is still objectively valid for orbiting space stations, since cargo ships continue to supply them with natural water, fresh vegetables and fruits, and unwillingly, a natural (Baikonur) atmosphere at each docking with cargo ships and visiting crew ships (together with their terrestrial microflora).

For open systems, the *a priori* suitability and adequacy of the natural environment to man's biological requirements, which results from man's prolonged adaptive evolution, was naturally taken as an empirical fact, an axiom of habitability.

But as we move to complete physicochemical regeneration of the atmosphere and water from products of man's vital activity, i.e., toward a completely artificial habitat, the original principle of the environment's *a priori* adequacy becomes invalid, since the suitability of an unnatural environment for prolonged human habitation is groundless. As a result, questions that science had

never had to face arose—what factors ensure the biological adequacy of the natural environment, in what phenomena and circumstances is it specified, how and which of them must be replicated in the artificial environment in order to make it biologically complete and suitable for prolonged habitation? Here we must take into account not only the direct, e.g. physiological, effect of environmental factors, but also their possible information (signal) value. Here we must recognize the considerable incompleteness of our knowledge of many factors in the natural environment, their significance for the human body, their necessity as constant environmental factors that make it biologically complete and biologically adequate for human needs.

The limitations of our knowledge about man's links to the natural environment can be seen in Table 1, where we tried to compare things in terms of the typical times over which the consequences of a disruption of the organism's links to a particular environmental factor are identified.

**Table 1. Typical Time for the Manifestation of Disruptions in an Organism's Natural Links to Habitat Factors**

Environmental factors	Time, hr
Respiratory gases	$n \times 10^{-2}$ (minutes)
Water	$n \times 10^1$ (days)
Food	$n \times 10^2$ (weeks)
Vitamins, microelements	$n \times 10^3$ (months, years)
	$n \times 10^N$ ( $N > 4$ ) (years, generations)

In connection with this table, it is noteworthy to mention that 19th-20th century science added only the fourth and last line, while all preceding ones were undoubtedly known even to stone age man, although without certain details. So we can assume that the table includes mankind's entire experience from prehistoric times.

The broken line in this table denotes the boundary of precise knowledge of basic vital factors in the environment subject to standardizing and monitoring for habitability. They cover only those links between the body and the environment whose disruption are identified within 2 percent of the length of man's life activity. However, this does not mean that nature does not contain other vital factors whose typical active life exceeds known limits and extends for years or a generation.

Still beyond the boundary of the concept of habitability are: geophysical fields—magnetic, gravitational, electrical; the constant formation and movement of various charged particles in the atmosphere (aero-ions) related to the electrical field; various aerosol particles—mineral, organic, biological (bacteria, spores, and plant pollen); and unfiltered atmospheric ultraviolet radiation (exciting a multitude of photochemical reactions with the formation of free radicals and other biologically active substances).

These are all actual constant factors of the natural habitat whose significance for the human body has barely been discovered. They have virtually been ignored as ecological factors of the natural environment. Beyond the boundary of precise knowledge is something critical from the standpoint of the theory of habitability—the biogenic, natural essence of the terrestrial atmosphere and water. The natural terrestrial atmosphere is qualitatively far removed from our surrogate model of the "space atmosphere" (nitrogen + oxygen + carbon dioxide); while natural water—hardly the only substance with the formula  $H_2O$ —in pure form, is extremely harmful to all organisms.

Of course science is aware of information about most of the factors not covered in the table, but this information falls into the sphere of interests of individual disciplines—the physics and chemistry of the atmosphere, hydrobiology, ecological physiology, medical geography, health resort treatment, etc. It has not been united into a single system of knowledge of natural factors of the human habitat or its terrestrial ecology, and it seems to be an important problem for the development of the future concept of habitability—the concept of human ecology.

In addition to the oxygen and carbon dioxide that we have standardized, normal components of the terrestrial atmosphere include many hundreds of organic substances of basically biogenic origin. They are the products of the vital activity of all terrestrial organisms, primarily plants and soil microorganisms. In traditional toxicology, they are usually called harmful impurities. We avoid this term, since there are no substances in nature that are absolutely harmful to man, only certain concentrations may be harmful (examples include mercury and arsenic used in medicine).

But no one had ever thought that these permanent and obligatory components of the natural atmosphere could be useful or necessary directly to man. Only N. G. Kholodnyy [20], who analyzed this problem scientifically, proposed calling substances released by plants into the atmosphere "atmovitamins". He hypothesized that these substances are found everywhere that there is rich, rapidly vegetating flora as well as in the soil atmosphere. Entering the body of an animal or a man through the respiratory tracts, atmovitamins perform certain physiological functions necessary for normal vital activity. Here again we have an example of a premature idea which is only now acquiring new resonance in terms of terrestrial human ecology. Further development of this idea must also be included into the program for creating the future concept of the habitability of extra-biospheric manned facilities for many years of self-contained existence. The total number of recorded volatile organic components in a biogenic atmosphere exceeds 400, and there is no reason to think that our knowledge of the atmosphere's organic composition is complete [9, 11].

These recorded, and even unrecorded, substances constitute the entire wealth of the terrestrial atmosphere's

organic composition, which distinguishes it from various surrogates in modern manned objects. Despite the extremely low concentration of organic components in the natural atmosphere, the total volume of their production may approach the annual production of the vegetative biomass. In terms of the magnitude and constancy of contact with terrestrial organisms, the atmosphere is a continuously active component of the habitat, while neither water nor food is. It is sufficient to recognize that more than  $5 \times 10^5$ /liter of air pass through the human lungs in a month.

Modern science has not studied these problems systematically nor raised them in theoretical terms. Only in health resort treatment have serious attempts been made to reinforce intuitive and empirical notions (even from Hippocrates' time) of the wholesome properties of natural factors by analyzing their physicochemical base; the positive role of aero-ions, aerosol, and ozone, and atmospheric electricity [3, 17] is also being studied along with the atmosphere's biologically active organic components [19, 20]. In addition to volatile components, the terrestrial atmosphere contains a large number of multi-molecule aggregates, both organic and inorganic—so-called aerosols, particles from submicron to micron size. In the submicron range, they detect both changes in physical properties, and increases in the chemical and catalytic activity of the basic matter [17]. If we add to this their ionization in the Earth's electrical field, this makes them aero-ions—an independent ecological factor of the environment for terrestrial organisms.

Finally, inorganic aerosols (terrigenic and oceanogenic), which are significant components of the natural atmosphere and are not taken into account in our habitability practice, are a source of aerogenic microelements consumed through the respiratory tract. This is why we cannot correctly determine the time constant for microelements (as in Table 1), as we do for other environmental elements which may be monitored if necessary.

The absolute values of biogenic and abiogenic emissions into the atmosphere presented in Table 2 are of interest.

**Table 2. Capacity (tons per year) of Certain Processes of Mass Transfer in the Biosphere [3]**

Vapors of natural or anthropogenic aerosol-forming substances	$1 \times 10^9$
Removal of ions with plant transpiration water	$1.2-1.4 \times 10^9$
Spores and pollen	$1.6 \times 10^9$
Volcanic discharges into the atmosphere	$2-3 \times 10^9$

Even a superficial survey of data on the physical, chemical, and biological components of the natural atmosphere shows more than just the complexity of its composition. It is quite clear that many paths in the biological and geochemical cycle in the biosphere pass through it and intersect, which also means the paths by

which diverse material relations of the organisms populate the land, in addition to their consumption or release of oxygen and carbon dioxide. Hence it should be clear that replacing the actual terrestrial atmosphere, of which we spoke, with a mixture of nitrogen, oxygen, and carbon dioxide means in practical cosmonautics only depriving man of the most direct, continuous link with the natural environment, while the natural atmosphere is an area of universal communication with terrestrial organisms and abiogenic processes regardless of whether modern science is aware of them or not.

Natural water is a complicated, multi-component body. All kinds of natural water on Earth are or were a habitat for various organisms, which makes it a unique "bio-inert" (according to V. I. Vernadskiy) body, whose many properties are totally connected with living matter. This is why water, recovered through different physicochemical methods, is unsuitable for water organisms even though it fully complies with GOST standards [2]. For this reason, public health hydrobiology formulated the concept, long ago, of biologically complete water [18], which is linked to the presence of biologically active products of the metabolism of hydrobiots (lipids, fatty acids, fat-soluble vitamins, free radicals, products of peroxide oxidation, etc.).

This incomplete survey of unrelated data on the features of the natural habitat show that our actual models of the environment in space objects are only primitive surrogates. It shows how complicated the natural atmosphere and natural water are in their composition and origins (biogenic and abiogenic), and how closely they are related to the activity of living organisms and are essentially inseparable from them.

Earth obviously has no other (non-biological) mechanisms which can reproduce the natural habitat in all its biological completeness. It is also obvious that, theoretically, man, like other organisms, is historically incapable of living in any other abiogenic environment longer than a limited time defined by the inertia of biological systems. This follows from the fact of organisms' adaptive evolution in their habitat and requires no experimental proof. This proof was provided long ago by the history of the biosphere; and the entire period of the development of man as a part and product of the biosphere, the entire period of the development and evolutionary strengthening of the unity of organism and habitat in the real, natural scientific, not philosophical, understanding served as a continuous experiment. Recognition of the practical strength of this principle of unity, recognition of man's place as a part and product of nature on Earth must underlie the initial fundamental principle of modern human ecology and the concept of habitability that emerges from it.

Scientific concepts do not develop instantaneously. They are formed when there is a need for them, as a result of scientific thinking and its grasp of new scientific facts. In this case the situation is as follows: In the imminent period of the transition to extra-biosphere facilities with

many periods of self-contained existence, there is also a need for a new concept of the human habitat that would encompass the largest number of facts about the unique features of nature on Earth which remain outside the concept of habitability which, while ambiguous, unquestionably has a role in modern space hygiene.

These notions about the environment and man's place in it make it possible to identify certain empirical positions which can be used as axiomatic bases for a future concept of habitability under the new conditions of its use—during the many years of man's isolation from the biosphere:

1. The inadequacy of our knowledge about man's natural habitat. It does not fully reflect its properties as a complex multi-component, biogenic, self-regulating and self-renewing system.
2. The environment is closely linked with living matter, which determines its biological completeness and *a priori* adequacy to organisms' needs, and fundamentally distinguishes it from any artificial abiogenic environment.
3. Terrestrial nature is the only evolution-tested environment *a priori* suitable for man's unlimited, long-term presence. Possible abiogenic environments do not possess this *a priori* suitability. Therefore, the environment is an absolute standard for the habitat of both man and other organisms.
4. Any artificial abiogenic environment has theoretical limitations in terms of habitability which are proportional to the degree to which it does not match the natural original.
5. In isolated manned facilities, the biological completeness of the habitat may be achieved only as a result of the action of the biological mechanisms by which it forms and similar mechanisms by which natural ecosystems function.

This environment approximates the natural environment, more fully meets man's biological needs, and is the only possible environment capable of providing him with optimum conditions during prolonged separation from the biosphere. These systems have no substitutes in the development and use of the resources of space.

Here we have come up against the link between the problem of habitability and human BLSS. BLSS can not only replicate the basic means of existence (oxygen, water, food) and remove carbon dioxide gas and other products of man's vital activity on the basis of the biological cycle of matter. The habitat created in them is biogenic in its origin and, therefore, can be theoretically close to the natural environment, despite our incomplete knowledge of its multitude of components. The task of supplying the crew's vital needs in space flight essentially involves creating an artificial system for cycling matter in which all man's material and energy demands are recorded with maximum precision.

For the first time man's existence, on this basis, depends on creating a situation in which the system's working capacity and viability become directly dependent on the activity of man as one of its functional units. This dependence is so great that our customary notion of a human life support system as something external to him ceases to be indisputable, since man is an object of support only in a system in which he himself is needed as an integral part of the system as a whole. The prototype of this system is nature on Earth, existing on the basis of a continuous transfer of elements from inert nature to the composition of living organisms and back.

Soviet science began work on BLSS 30 years ago in connection with conquering space. Our research has made the general principles for the structure of these systems [12, 13] sufficiently clear, their functional and biocenotic structure, the characteristics of the main functional units in the system, the basis for the closed process of these units, and ways to increase the degree to which the systems are closed.

The result was the development of ground-based BLSS models based on the activity of unicellular algae, higher plants, and microorganisms using certain physicochemical processes to return several products from organic wastes to the cycle. They demonstrated the BLSS' capacity for relative independent existence if the number of kinds and the weight of living matter in the limited space typical for space objects is restricted. This stability was accomplished through the internal mechanisms of the system itself with minimum intervention from outside. The system's stability, as well as the number of functions to be performed (some unplanned) indicates that these models possess characteristics of a closed ecological system. These models confirmed that the approach and understanding of the basic principles for creating closed ecological systems are correct and demonstrated the theoretical possibility of extended support for human activity cut off from the terrestrial environment [8, 12, 13].

How completely man's needs are met and the quality of life on space station will, for a long time, depend on the limited capabilities of space technology, and we will have to deal with the primacy of technical limitations for a long time. But, theoretically, this primacy is temporary. The inevitable increase in the technical, including energy, potential of cosmonautics is reducing the strength of this primacy and leading to a gradual increase in the primacy of man as the sole subject of space activity. For this reason the problem of habitability as an important part of the science of man will concentrate in itself an increasing amount of knowledge, both about man and about his natural habitat.

Solving the problem of habitability requires that data from various fields of space (marine, etc.) medicine—traditional hygiene and physiology, immunology, epidemiology, psychophysiology, and social psychology—must be combined with data from the physics, chemistry, and biology of the atmosphere and water as

basic components of the habitat, which results in the development of a complete science—human ecology.

Today the main point is becoming clear: human space activity of any duration is possible. The more representative a portion of the Earth's biosphere that can be embodied in actual BLSS, the longer man can be separated from his links with terrestrial conditions. Biosocial and psychosocial aspects of the problem, whose limiting value will increase as time in isolation from Earth continues, are still beyond analysis. However, to take advantage of this research requires a new experimental base and accelerated research, since it is inevitably prolonged because of the specifics of the object of study, while the time available to carry out BLSS projects can only diminish. Today the most correct strategy in the development of BLSS would be to develop combined systems based on physicochemical and biological processes in which the percentage of the latter would gradually increase as the capabilities of space technology increase.

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UDC 577.152.314.1:579.873.71

**Strain *Streptomyces Fradiae*, Producer of Restriction Endonuclease SFR 274 I**

907C0663A Novosibirsk IZVESTIYA SIBIRSKOGO OTDELENIYA AKADEMII NAUK SSSR: SERIYA BIOLOGICHESKIH NAUK in Russian No 1, Apr 90 pp 32-34

[Article by L. I. Puchkova, G. N. Krivopalova, I. S. Andreyeva, et al., NIKTI BAV NPO "Vektor" Ministry of the Medical and Biological Industry, USSR, Berdsk]

[Abstract] An attempt to detect new promising restrictionase producers among strains of the *Streptomyces* genus used strains of *S. fradiae* Ac 149 and *S. lavendulae* S-494. Strain *S. fradiae* Ac 149 proved to be a promising restrictionase producer, recognizing sequence CTCGAG. It may replace *Xho* I and *Sla* I in experiments involving fragmentation of DNA in genetic engineering studies. Figure 1; references 9: 4 Russian, 5 Western.

UDC 579.68.023.12(282.256.3)

**Appearance of Producer-Strains of Restriction Endonucleases Among Aquatic Microorganisms of Lake Baykal**

907C0663B Novosibirsk IZVESTIYA SIBIRSKOGO OTDELENIYA AKADEMII NAUK SSSR: SERIYA BIOLOGICHESKIH NAUK in Russian No 1, Apr 90 pp 35-37

[Article by V. S. Dedkov, V. Ye. Repin, N. I. Rechkunova, et al., NIKTI BAV NPO "Vektor," Ministry of Medical and Biological Industry, USSR, Berdsk; Limnological Institute, Siberian Department, Academy of Sciences, USSR, Listvyank]

[Abstract] Detection and identification of new producer-strains of restrictionases among microorganisms of the unique ecological niche Lake Baykal were described. Water samples were taken from different depths in different parts of the lake, from bottom deposits, and along the shore. Bacterial strains *Flavobacterium aquatile*, *Hafnia alvei*, *Acinetobacter calcoaceticus*, and *Pseudomonas gladioli* were producers of restrictionases Fau I, Hal I, and Hal II, Aca I, and Pga I, respectively. The producer-strains that are detected are cultivated readily and may be suitable for industrial production of restrictionases. Figure 1; references 10: 6 Russian, 4 Western.

UDC 577.152.314.1

**Establishment of Specificity of Restriction Endonuclease Bse 21 I**

907C0663C Novosibirsk IZVESTIYA SIBIRSKOGO OTDELENIYA AKADEMII NAUK SSSR: SERIYA BIOLOGICHESKIH NAUK in Russian No 1, Apr 90 pp 138-139

[Article by S. Kh. Degtyarev, A. A. Kolykhalov, V. Ye. Repin, et al., All-Union Scientific Research Institute of

Molecular Biology, NPO "Vektor," USSR Ministry of the Medical and Biological Industry, Koltsovo]

[Abstract] A study of bacterial strains isolated from natural isolates revealed the strain *Bacillus species* 21, from which restrictionase endonuclease Bse 21 I was isolated. Restrictionase Bse 21 I recognizes the sequence CCT-NAGG with the cleavage point between C and T. Restrictionase Bse 21 I is an isoschizomer of Sau I and may be used extensively in structural and functional studies of DNA. Figure 1; references 4: Western.

UDC 577.152.321.088.1:579.852.11

**Detection of Virus-Synthetic Polyelectrolyte Complexes by Antibodies**

907C0733A Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 311 No 6, Apr 90 pp 1482-1486

[Article by B. B. Dzantiyev, A. N. Blintsov, V. A. Izumrudov, A. B. Zezin, A. F. Bobkova, A. M. Yegorov, I. G. Atabekov, corresponding member, USSR Acad. Sci., and V. A. Kabanov, academician, Institute of Biochemistry imeni A. N. Bakh, USSR Academy of Sciences, Moscow; Moscow State University imeni M. V. Lomonosov]

[Abstract] As part of the research on novel immunochemical techniques, a system was developed for virus analysis relying on precipitation of virus-labeled antibody complexes by synthetic polyelectrolytes. Studies with a number of plant viruses (tobacco mosaic virus, potato X virus, and potato leafroll virus) demonstrated that essentially 90 percent virus precipitation was attainable within one minute, with addition of equimolar concentrations of reagents in the following sequence: (virus + polycation) + polyanion. Detailed investigations with the potato X virus bound to antibodies labeled with horseradish peroxidase and subsequently sequestered into an insoluble stoichiometric complex formed by sodium polymethacrylate (polyanion) and poly-N-ethyl-4-vinylpyridine bromide (polycation) confirmed the utility of this approach as a practical technique. The reactions were carried out at 20°C in 0.01 M potassium phosphate buffer, pH 7.8, supplemented with 0.1 M NaCl and 0.1 percent Tween-20. Figures 4; references 10: 7 Russian, 3 Western.

UDC 575.224.4+577.963.3

**In Vivo Site-Directed Mutagenesis and Antisense Inhibition of Adenovirus SA7 Oncogene Integrated in Rodent Cell Lines Transformed by Polyalkylating Oligo/Polymer Derivatives**

907C0733B Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 311 No 6, Apr 90 pp 1487-1491

[Article by V. I. Pantin, G. Ya. Solovyev, N. V. Sats, V. L. Surin, Ye. L. Zhukova, T. B. Borovkova and N. I. Grineva, Scientific Research Institute of Experimental

Hematology and Biotechnology, All-Union Hematological Scientific Center, Moscow]

[Abstract] An investigation was conducted on the effects of oligo/polynucleotides representing regions of single-stranded DNA of phage M13 and bearing Ela and E1B regions of monkey adenovirus SA7/S-16/, as well as their polyalkylated derivatives, on malignant rodent cells transformed by the adenovirus SA7 oncogene. The studies were performed on rat SH2 cells and mouse G11 cells; the polyalkylated reagents carried 4 percent of the alkylating groups along the nucleotide backbone. Incubation of the target cells with the reagents for 1 - 2 h at 37°C led to alterations in cellular morphology and recovery of normal phenotype only with the site-directed reagents. The frequency of changes ranged from 17 - 26 percent in the case of the SH2 cells and from 5 - 8 percent for the G11 cells. Blot hybridizations of pre- and post-treatment G11 cells demonstrated that the target sites consisted of the viral DNA regions in the genome of the transformed G11 cells. In vivo mutagenesis was accompanied by antisense inhibition of Ela expression. Polyalkylated derivatives of +chains of the oncogene evoked maximum (approximately 80 percent) mutagenesis and a minimum of antisense inhibition, whereas unalkylated oligo/polynucleotides had the reverse effect—maximum inhibition (approximately 60 percent) and minimum mutagenesis. Figures 1; tables 2; references 15: 7 Russian, 8 Western.

UDC 577.152.2

**Recombinant RNA-Dependent DNA-Polymerase RSV. Isolation and General Characteristics**

907C07974 Moscow BIOKHIKIYA in Russian Vol 55 No 4, Apr 90 pp 586-594

[Article by A. P. Chernov, A. A. Melnikov, V. V. Shmatchenko and I. Fodor; Institute of Biochemistry and Physiology of Microorganisms, USSR Academy of Sciences, Pushchino, Moscow Oblast]

[Abstract] Isolation of recombinant reverse transcriptase RSV and determination of its characteristics, the comparison of it with preparations of reverse transcriptases isolated from RSV virus and the determination of the suitability of the recombinant reverse transcriptase for genetic engineering were described and discussed. Recombinant reverse transcriptase RSV preparations were isolated from *E. coli* HB101/pMF14 cell cultures. Purified up to a homogeneous state, the enzyme consisted of 2 subunits with molecular masses of 9/ + or - 4 kDa and 61 + or - 3 kDa. Comparison of the enzymic characteristics of recombinant transcriptase with characteristics of the enzyme isolated from Rauss sarcoma virus indicated that the recombinant reverse transcriptase in the preparations obtained exist in a subunit form,  $\alpha\beta$ , and form a relatively stable form,  $\alpha_2$ . Figures 6; references 13: 3 Russian, 10 Western.

UDC 573.3

**Modification of Liquid Crystalline Structure of DNA by Natural Compounds**

907C0732A Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 311 No 4, Apr 90 pp 980-983

[Article by S. G. Skuridin, V. K. Rybin, A. T. Dembo, N. S. Badayev and Yu. M. Yevdokimov, Institutes of Molecular Biology imeni V. A. Engelhardt and of Crystallography imeni A. V. Shubnikov, USSR Academy of Sciences, Moscow; Moscow State University imeni M. V. Lomonosov]

[Abstract] Circular dichroism (CD) spectra, polarization microscopy, and x-ray analysis were employed in assessing changes in DNA-stellin B liquid crystals (formed in salt solutions containing polyethylene glycol) to assess the effects of tryptic digestion of stellin B. The

CD spectra revealed that in the dispersed cholesterol-like liquid crystalline phases formed at ' $r$ ' < 0.15, the stellin B molecules function as counter-ions providing additional shielding for DNA phosphate groups. In addition, the decrement in the amplitude of the negative band at ' $r$ ' < 0.15 indicates that stellin B crosslinks DNA molecules. X-ray scatter at ' $r$ ' = 0.6 provides further evidence of liquid crystal packing of the DNA-stellin B complexes with a 'nonspecific' texture. Trypsin treatment of the complexes leads to breakdown of the crosslinks between DNA molecules and formation of cholesterol-like liquid crystals with a 'fingerprint' texture. Addition of trypsin inhibitor (diisopropylfluorophosphate) counteracted the trypsin-induced changes. The fact that trypsin concentrations as low as  $10^{-13}$  to  $10^{-14}$  M induced detectable changes in the DNA-stellin B liquid crystals indicates that such crystals offer promise as extremely sensitive biosensors for proteolytic enzymes. Figures 3; references 10: 4 Russian, 6 Western.

UDC 615.357:577.175.322/012.6

**Medicinal Form of Genetic-Engineered Somatotropin**

907C06654 Moscow FARMATSIYA in Russian Vol 39 No 2 Mar-Apr 90 pp 37-40

[Article by G. K. Korotayev, T. I. Lys, L. G. Makarova, et al., All-Union Scientific Research Institute of Biotechnology, Moscow]

[Abstract] Creation of a stable medicinal form of genetic-engineered somatotropin and standardization of its quality involved the following steps: preparation of 0.05 M of an ammonium hydrocarbonate solution, preparation of a 1 percent solution of mannite in the ammonium hydrocarbonate solution, preliminary filtration of the solution obtained through a packet of filters and a membrane filter with pore size of 0.8 - 0.45 µm, preparation of a 0.1 percent solution of genetic-engineered somatotropin in the filtrate obtained, sterile filtration through a membrane filter with a pore size of 0.22 µm, pouring into 1- or 2-ml flasks or vials (2 or 4 effective dose respectively), freezing, hardening, sublimational drying, corking, and preparation of finished product. The product (somatogen) is a white powder, soluble in water and in a 0.25 percent solution of novacaine. Its solubility, transparency, chromaticity, pH, toxicity, and sterility met the standards of the quality required, and these standards were unchanged during storage of 2.5 years. References 13: 7 Russian, 6 Western.

**Bacterial Test System for Mutagens Developed**

907C0731B Moscow PRAVDA in Russian 20 Jul 90 Second Edition p 4

[Article by A. Kunarev, candidate of technical sciences, manager of The Fund For Ecological Inventions at USSR Ecofund: "Genes Send an 'SOS'"]

[Text] The most fearful aspect of the impending ecological catastrophe is its influence upon human heredity. Humanity may simply degenerate or die out if timely measures are not taken. Alas, there is support for this statement: The number of newborns with genetic deviations from the norm is increasing. Changes in the hereditary mechanism are caused not only by the various harmful emissions and toxic discharges from industrial enterprises, that is, the wastes from our activities. It turns out that the enterprises are producing products that are in themselves harmful to health.

Every year scientists discover thousands of new chemical compounds in their laboratories.

How can one recognize harmful substances that have an effect upon heredity? Scientists have turned to genes themselves to answer this question. By using genetic engineering methods, additional genes have been "sewn" onto the hereditary apparatus of certain species of bacteria. As a result of this operation, the bacteria with the

"modernized" genetic apparatus have acquired the capability of sending an "SOS" when they interact with the dangerous substance being studied. So now, prior to the construction and even the design of factories, one can, at the laboratory synthesis stage, determine whether a new substance is dangerous to all life forms.

In many countries, work is under way creating bacterial systems for testing mutagens. In the USSR such a system has been developed at the Institute for General Genetics imeni N. I. Vavilov and at the Scientific Research Institute for Bacteria and Serums with the assistance of the MOST [Not further identified] Young Student Center.

The system was displayed at "Healthcare-90", an international exhibition recently held in Moscow. Visitors were greatly interested in this development because our system is an order of magnitude less costly than similar test systems from France and Japan. Also, it quickly provides a diagnosis; it is technically simple, easily automated, and very sensitive to mutagens; and it determines the mutagenic and carcinogenic activity of practically any substance, either organic or inorganic. By using the system we can recognize harmful substances throughout the entire country.

UDC  
579.842.11:[579.222:[547.581.2+547.551.1+547.56]**Reduction of Nitro Derivatives of Benzoic Acid, Phenols and Anilines by E. coli Cells**

907C0812C Moscow KHIMIKO-FARMATSEVТИЧЕСКИЙ ZHURNAL in Russian Vol 24 No 4 Apr 90 pp 54-57

[Article by T. I. Davidenko and G. I. Bondarenko, Physico-chemical Institute imeni A. V. Bogatskiy, UkrSSR Academy of Sciences, Odessa]

[Abstract] A study of the reduction of nitro-substituted benzoic acids, phenols and anilines with *E. coli* cells showed that *p*-, *m*-nitrobenzoic acids, *m*-nitroaniline, *m*-, *o*-nitrophenols are reduced by *E. coli* cells with formation as single products of reaction of corresponding amides with yields of 23 - 75 percent. *o*-nitrobenzoic acid, *n*- and *onitroanilines* and *n*-nitrophenol were not reduced. Kinetic parameters for their reduction were defined. There were no dependences of kinetic characteristics of the process on the lipophilicity constant (*IgP*). The values of kinetic parameters of reduction of *n*-nitrobenzoic acid by native and immobilized cells were similar, indicating the mild nature of immobilization of *E. coli* cells in carrageenan. *V<sub>max</sub>*, *E. coli* cells, immobilized on carrageenan reduced *n*-nitrobenzoic acid by using columns with inactivation half-life up to 155 hours. The study showed that reduction of nitro-substituted benzoic acids, phenols and anilines by *E. coli* cells and their forms immobilized in carrageenan proved to be a promising method of producing *o*- and *m*-aminophenol, *m*-phenylenediamine,

*n*-aminobenzoic acid, produced by multi-stage chemical synthesis at high temperature and pressure. Figures 2; references 12: 8 Russian, 4 Western.

UDC 615.31:547.458].012.6

**Sorption Immobilization of Yeast Cells of Polysaccharide Producers**

907C0812D Moscow

*KHIMIKO-FARMATSEVTICHESKIY ZHURNAL*  
in Russian Vol 24 No 4, Apr 90 pp 57-59

[Article by G. A. Yaskovich, L. V. Dmitriyenko, G. E. Yelkin et al.; Chemico-pharmaceutical Institute, Leningrad]

[Abstract] A study of equilibrium characteristics of sorption immobilization of yeast cells of polysaccharide

producers on porous carriers of different structure and a check of the biosynthetic activity on the immobilized producers involved the use of Cr. laurentii 1803, Cr. albidus 1643, Bullera alba BKMY-2141, Cr. luteoulus IFO-0411 and Cr. humicolus BKMY-984. Cells were immobilized on the following carriers: SKH-4M hemosorbent, KC-41 ceramic carrier, elastic polyurethane foam, AMP macroporous anionite, alginate fiber and porous keramzit. The Langmuir isotherm equation was used to depict sorption immobilization of the yeast cells. Constants of sorption immobilization and values of limiting sorbent capacitances were calculated. The energy of cell population-carrier interaction was 69 - 72 kJ/mole. The carrier and the binding process produced no effect on morphological indicators of the absorbed cells. Biosynthetic activity of the absorbed cells persisted for a long time. Figure 1; references 13: 8 Russian, 5 Western.

UDC 616.98:578.833.29j-036.22(470.46)

**Crimean-Congo Hemorrhagic Fever Cases in Astrakhan Oblast**

907C0856C Moscow VOPROSY VIRUSOLOGII in Russian Vol 35 No 3, May-Jun 90 pp 228-231

[Article by S. Ye. Smirnova, A. G. Sedova, Yu. V. Zimina, and A. S. Karavanov, Poliomyelitis and Viral Encephalitides Institute, USSR Academy of Sciences, Moscow; Astrakhan Oblast Sanitary and Epidemiological Station]

[Abstract] The results of Crimean-Congo hemorrhagic fever (CCHF) cases recorded from 1980 through 1987 are reported and include clinical, serological, epidemiological, and virusological data. Morbidity with CCHF is

sporadic, but patients with marked hemorrhaging frequently initiate intrafamily or intrahospital outbreaks with a high mortality rate. No outbreaks of this disease have been recorded in the USSR within the last 10 years, but strains of the etiological agent responsible for this infection are constantly being isolated from ticks in Kazakhstan and the central Asian republics. Included in the study were 74 people with acute fever diseases, ten of which were diagnosed with CCHF. All of these cases resulted from tick bites or crushing the ticks with unprotected hands after removing the insects from their pets. Also included in this report is an evaluation of techniques for diagnosing CCHF. The findings suggest that not only is there an active CCHF focus in Astrakhan, but that the isolated cases of CCHF reported from 1980 through 1987 do not reflect the actual morbidity level of this disease. Tables 3; references 21: 8 Russian, 13 Western.

UDC 591

**Integration and Expression of  $\beta$ -Casein Gene of *Bos Taurus* in Transgenic Rats and Mice**

907C05904 Moscow ONTOGENEZ in Russian Vol 21 No 2, Mar-Apr 90 pp 215-218

[Article by D. V. Mukha, S. I. Gorodetskiy, T. V. Ignatyeva, and A. P. Dyban, Institute of General Genetics, USSR Academy of Sciences]

[Abstract] The feasibility of producing transgenic rats was studied. Expanding the number of species of laboratory animals that are used for producing transgenic specimens may make it possible to reveal new mechanisms for regulating gene activity. The integration and expression of the *Bos taurus*  $\beta$ -casein gene in transgenic rats and mice was studied.  $\beta$ -casein is the main protein in mammalian milk. Due to the location of the tissue-specific regulatory elements of *Bos taurus*  $\beta$ -casein is

not known, the genome gene of  $\beta$ -casein with its flanking sections is used as the foreign DNA. The KpnI fragment of the clone containing the  $\beta$ -casein gene was used for microinjection into the male pronucleus. Three transgenic rats and two transgenic mice were obtained. Both transgenic mice contained the complete *Bos taurus*  $\beta$ -casein gene in their genome, while only one of the three rats contained it. Analysis of the progeny of the rats and mice showed that the *Bos taurus*  $\beta$ -casein gene is not only integrated into the genome, but is also transferred by inheritance and is found in about 50 percent of the  $F_1$  progeny. Expression of the *Bos taurus*  $\beta$ -casein gene was studied in  $F_1$  females obtained by crossing the transgenic male and Wistar females. The transgenic females were sacrificed on the eighth day of lactation. Expression of the *Bos taurus*  $\beta$ -casein gene was not found in the mammary gland during lactation (tissue-specific expression) or in other organs in all of the animals studied. Possible reasons for this are presented. Figure 1, references 17: 4 Russian, 13 Western.

UDC 612.017.06:613.2].08

**State of Some Indicators of Immunological Reactivity (Humoral Link) in Persons Exposed to Food Products Contaminated by Mycotoxins**

907C07894 Moscow VOPROSY PITANIYA in Russian No 3, May-Jun 90 pp 31-35

[Article by K. R. Dadiani, N. Ye. Voytko and V. A. Tutelyan; Scientific Research Institute of Sanitation and Hygiene imeni G. M. Natadze; Georgian SSR Ministry of Health, Tbilisi; Institute of Nutrition, USSR Academy of Medical Sciences, Moscow]

[Abstract] A study of blood serum levels of immunoglobulins of five basic classes (G, M, A, D and E), of titers of complement components: C1-inhibitor, C3, C4, C5, C9; and also the levels in the blood plasma of haptoglobin, orosomucoid, transferrin, ceruloplasmin,  $\alpha_1$ -antitrypsin,  $\alpha_2$ -macroglobulin, albumin and prealbumin in persons exposed, in their work, to the raw material of food contaminated by mycotoxins, used the method of immunodiffusion on agar with the use of specific antisera and IgE concentration was determined by radioimmunosorption. Subjects of study included 50 persons who had worked at grain treatment plants from 1 - 15 years. Long term contact with food and fodder products containing mycotoxins caused increase of the IgE level and a decrease in IgG level, and reduced the concentration of the complement components C3 and C9, transferrin and orosomucoid. Thus, long contact with mycotoxin-contaminated industrial raw material produced changes in the blood serum immunoglobulin spectrum, the complementary fractions level and in the plasma protein fractions which play an important role in the immune response of the organism. Figure 1; references 13: 3 Russian, 10 Western.

UDC 616.98:578.832.1]-092.9-0:615.275.4]-07

**Immunostimulating Effect of Mytilan Following Experimental Influenza Infection**

907C08564 Moscow VOPROSY VIRUSOLOGII in Russian Vol 35 No 3, May-Jun 90 pp 194-197

[Article by A. V. Tsybulskiy, R. G. Ovodova, V. Ye. Glazkova, N. N. Besednova, Yu. S. Ovodov, T. G. Orlova, O. N. Shcheglovitova, and L. A. Minskaya, Epidemiology and Microbiology Scientific Research Institute, Siberian Division, USSR Academy of Medical Sciences, Pacific Institute of Bioorganic Chemistry, Far East Division, USSR Academy of Sciences, Vladivostok; Epidemiology and Microbiology Scientific Research Institute imeni N. F. Gamaleya, Moscow]

[Abstract] The protective effect of the natural biopolymer mytilan, a preparation obtained from the commercially harvested marine invertebrate *Crenomytilus grayanus*, following experimental influenza infection (strain A/Aichi/68(H3N2)) was studied on inbred and outbred male mice (16 - 18 g) and guinea pigs (400 - 450 g). The animals were infected intranasally with the influenza virus (0.5, 1, 10, and 100 LD<sub>50</sub> in 0.02 ml physiologic solution). Mytilan was administered subcutaneously, intraabdominally, and intranasally at various periods and in various doses, with subcutaneous and intranasal administration shown to be most effective, protecting up to 60 percent of the animals. The results demonstrate that mytilan has a number of effects. It induces interferon synthesis in low titers, has a marked effect on flu virus reproduction, stimulates synthesis of specific anti-flu antibody-antihemagglutinins, and increases titers of specific antibodies to the flu virus. A 25 mg/kg dose of mytilan administered intraabdominally enhanced expression of Fc<sub>y</sub>-R and C3-R receptors on murine splenocyte membranes and increased the percentage of E-A rosette-forming peritoneal macrophages. The oxydation-reduction activity of guinea pig alveolar macrophages increased 2.1 times, 24 h after intranasal administration of mytilan in a 25 mg/kg dose, while hemotaxis of peritoneal macrophages also was enhanced. These findings indicate that mytilan suppresses virus reproduction and it has an immunostimulating effect that helps localize the process and decrease the mortality rate. Figures 3; tables 1; references 21: 17 Russian, 4 Western.

**Amniotsen Biostimulator Tested**

907C0710A Moscow RABOCHAYA TRIBUNA  
in Russian 12 May 90 p 4

[Article by O. Grabovskiy: "Bestowing Health"]

[Text] A medicine contained in man himself, a unique preparation, has been given the name amniotsen. It was developed by N. Reilyan, the chief physician of the Moldavian Republic Medical-Pedagogical Center of Marriage and Family. Patients of the Tiraspol Hospital for Invalids of the Great Patriotic War became the first people in general medical practice to test the preparation on themselves.

Those of them who wound up in the Saratov hospital in those hard times remember how astonishingly quickly casualties recovered here. Professor N. Krauze grafted pieces of fetal membrane tissue from parturient women onto them. It turned out that this tissue possesses powerful biostimulatory properties.

"Perpetuating the human race, the mother gives to the child a particle of herself, the best strengths of the body," explains the author of the innovation, Nikon Semenovich Reilyan. "They are concentrated in the placenta in the form of a highly rich assortment of valuable biologically active substances."

Amniotsen has proven itself well as an anti-inflammatory and as a tissue resorbing and generating agent. It was first used successfully to treat gynecological and urological diseases, sexual pathology and infertility. But it was found in this case to heal ulcers, resorb scars and benign tumors and even cause hair to grow back in the patients.

It goes without saying that the preparation is needed right now by many people. But this preparation is made by the republic center itself, in a specialized laboratory that can manufacture only 30,000 doses per year. And this is clearly not enough. Of course, an experimental production operation was organized at the Kishinev "Farmako" Plant. Special capacities producing six million doses a year were created there. But the equipment is standing idle due to a shortage of raw material.

At the same time placentas are being regularly collected from all maternity hospitals in major cities of our country's European territory, and two refrigerator cars filled with them are dispatched abroad every day—destined for style-conscious women in Paris. In France, where our placentas are sold for next to nothing, they are used to make cosmetics.

UDC 616.127

**The Prevention of Ischemic Heart Disease in Military Personnel**

917C0236A Moscow VOYENNO-MEDITSINSKIY ZHURNAL in Russian No 10, Oct 90 pp 36-38

[Article by Retired Major General K. G. Alekseev, Candidate of Medical Sciences]

[Text] Ischemic heart disease is one of the Army's and Navy's most pressing problems. Its prevalence for the past 5 years has increased overall among officers across the Armed Forces by 23.8 percent, and at the same time it increased among the Land Forces by 39.1 percent. It also increased in other types of armed forces, and remained at practically the same level in the Air Force. The latter may be due both to the requirements for professional selection as well as to more careful diagnosis of this illness, which in aviation leads to the removal of aviators from professional activities. The prevalence of IHD is uneven in relation to various districts. It was highest in 1988 in the Far Eastern Military District, the Northern Caucasus Military District, the Baltic Military District; and least in the Siberian Military District, the Turkestan Military District, the Western Forces Group, and the Black Sea Fleet.

Different approaches to the diagnosis of IHD in the process of the in-depth medical examination of officers and warrant officers in the dispensary can influence its prevalence; however, there can be no doubt about its increase; this is confirmed both by the hospital examination data and the increase in the number of lost workdays due to this illness. This phenomenon reflects the dynamics in the country as a whole. Thus, according to information from the USSR Ministry of Health, the prevalence of IHD from 1980 through 1987 increased by a factor of 2.5, and that of hypertensive disease by a factor of 2.

The risk factor concept, which is accepted by the overwhelming majority of researchers, is the theoretical and practical basis of the prophylaxis of IHD. Some factors which relate mainly to the male sex are: hereditary predisposition, disturbances in lipid and carbohydrate metabolism, arterial hypertension, tobacco smoking, insufficient physical exercise, frequently recurring mental and emotional tension, decreased tolerance for carbohydrates, etc. The observation of patients over many years has shown that changes at the molecular level in the endothelium of the wall of blood vessels, changes in the mechanisms of thrombus-formation, and vascular spasms may also be included here.

According to the data of one research group in the United States (1978), the widely known risk factors constitute approximately half of the total number. Disturbances in lipid metabolism (hypercholesterolemia), arterial hypertension, and tobacco smoking play a principal role in the development of IHD. The combination of these factors and their combination with other factors

increases the risk of illness even more. For example, the combination of hypercholesterolemia and tobacco smoking and excessive body weight increases the possibility of the development of IHD severalfold.

Hypercholesterolemia is usually combined with a decrease in the level of high density lipoproteins (alpha-cholesterol) and an increase in the content of low density lipoproteins (beta-cholesterol). The detection of hypercholesterolemia in the process of the annual in-depth medical examination is the basis for the assignment of these individuals to the high risk group for this disease. Various screening methods for the determination of blood cholesterol have been proposed to simplify mass examinations.

A bloodless instantaneous method for the indication of the cholesterol content in the skin, which directly reflects the degree of atherosclerotic damage to vessels, has been developed at the All-Union Scientific Research Institute of Physicochemical Medicine. The method is very simple: Three drops of the reagent of different concentrations, are applied to the subject's palm, incubated for one minute, and washed with water, then a special solution is applied to the same areas of skin. If all three spots are stained after 30 sec, this indicates pathological hypercholesterolemia (atherosclerosis at the clinical stage). The presence of two spots indicates that the patient should be assigned to the risk group. The appearance of one spot is considered the norm. According to the data obtained, the test indices correlate with the level of cholesterol and with the degree of atherosclerotic damage to vessels.

A method, using the original Soviet-produced "Zond-1" fluorimeter, for the determination of total blood cholesterol and triglycerides in a drop of blood was also developed by the same institute for mass testing. Testing has shown that one laboratory assistant can test 60 - 80 individuals in 4 h.

The organizing role of the medical service is extremely important in the total program of the campaign to establish a healthy way of life, an integral part of which is the prophylaxis of IHD. Among the specific prophylactic measures, those which are directed toward the elimination or mitigation of the principal risk factors should be singled out first of all. Influencing the main risk factor, the disturbance in lipid metabolism, is a difficult task, but is achievable with a certain degree of persistence. Various approaches along these lines are possible: the normalization of body weight, balanced nutrition with the introduction into the diet of products rich in polyunsaturated fatty acids, with a limited content of dietary cholesterol, and systematic physical activities which are appropriate in their demands.

Physical training, not with the aim of achieving a high level of athletic results, but for its general health and generally strengthening effect, is assigned a leading role in the prophylaxis of some cardiovascular diseases. The physician should form an opinion regarding the need for

constant improvement of physical development, intelligently utilizing the publicity such "miracle-working" systems of physical training as the Indian hatha-yoga, ushu gymnastics, aerobics, culturism, etc. As he gets away from sloganizing physical culture, each service person should be introduced to the knowledge of the principles of physical training, the persistent habit of daily physical exercises, and should skillfully learn the methods of monitoring his own condition. Physical exercises lead not only to normalization of metabolic processes, but of arterial pressure as well, thus exerting a favorable influence on the organism in the initial stages of hypertensive disease.

At the present time hypocholesterolemic agents such as clofibrate, miscleron, and nicotinic acid are practically not prescribed due to the negative side effects associated with prolonged use. The foreign preparations, hemifibrosil and lovastatin (mevacor), which have been undergoing clinical trials, merit attention. The latter has been tested in the USSR. It is effective, convenient for use (one tablet a day), and, according to preliminary data, does not manifest side effects. In the case of a high level of hypercholesterolemia, especially in the so-called homozygous form, extracorporeal blood purification is used, which is, however, more a treatment than a prophylactic method. In our view, a promising method has been developed for the elimination of hypercholesterolemia indirectly through the synthesis of high density lipoproteins (HDL).

The role of arterial hypertension as an IHD risk factor has been established, but the effectiveness of long-term antihypertensive prophylaxis to prevent this disease has been subjected to ever greater doubt. Many observations of Soviet and foreign authors demonstrate that antihypertensive agents reduce the frequency of cerebral disturbances and mortality from stroke, but do not significantly influence IHD mortality. The reasons for this paradoxical fact have not been sufficiently studied. The possibility has been hypothesized of a negative effect of hypotensive therapy on coronary circulation, in particular on coronary perfusion, as well as on an increase of atherogenic lipoprotein fractions when some hypotensive preparations are used (diuretics, especially of the thiazide series, beta-blockers). The unfavorable effect of a decrease in tolerance to carbohydrates under the influence of hypotensive agents cannot be excluded.

Thus, the role of antihypertensive preparations in the prophylaxis of IHD will be subjected to further study, including those agents which do not possess an atherogenic effect (calcium channel blockers, inhibitors of angiotensin-converting enzyme of the captopril type, blockers of alpha-1-adrenoreceptors, prazosin, etc.). On the basis of the data cited, monitoring the state of lipid metabolism and myocardial function (by echocardiography) is desirable during long-term antihypertensive treatment.

Antismoking propaganda has clearly been underestimated in the prophylaxis of IHD. The number of

smokers in the country, as well as in the Armed Forces, remains high, up to 40 - 50 percent and higher. The campaign against smoking is carried on more actively in the United States. The number of smokers among the country's white population has decreased almost four-fold in the last 20 years, from 60 percent to 16 percent (Z. Sadovskii, 1989). According to the report of J. A. Ballweg and coauthors (1989), in the United States the number of service persons who are smokers (smoking in the army is significantly more widespread than among the civilian population) decreased from 1980 through 1985 from 53 percent to 46 percent, mainly due to individuals aged 20 - 29 years. This indicates that antismoking propaganda can be effective.

The work experience of the medical service has shown that the primary prophylaxis of IHD, as of atherosclerosis generally, in the military collectives is most workable on the selective principle, i. e., in the first place among individuals carrying a burden of risk factors, especially in combination. It is necessary to distinguish such groups in the process of in-depth medical examination. A population-oriented program of prophylaxis, encompassing all the contingents, can be the next stage. In some countries, the United States for example, several national programs dealing with this problem have been adopted.

The secondary prophylaxis of IHD and other atherosclerotic diseases of the vessels has been directed toward the prevention of the progression of the disease, taking into account not only traditional risk factors, but the characteristics of its course as well, such as disturbances in cardiac rhythm, cardiac insufficiency, various accompanying diseases, etc. If non-pharmacological means are the basis of the primary prevention of IHD, the secondary prophylaxis of IHD is most often carried out using medicinal preparations.

The advisability of the comprehensive prophylaxis of IHD and other atherosclerotic diseases of the vascular system has been confirmed by the results of numerous Soviet and foreign cooperative investigations (A. M. Kalinina, et al., 1989; N. V. Perova, 1989; V. Conner and J. Bristow, 1986; and others). The data of the report of WHO experts on the dynamics of the mortality from cardiovascular diseases in a number of industrially developed countries for men in the 40 - 69 year age range are instructive (1988). The standardized mortality rates decreased in a decade by 25 - 36 percent in countries (Japan, Australia, USA, Canada, and others) in which national programs of prophylaxis have been adopted and implemented, which attests not only to the effectiveness of the prophylactic measures, but also to the successes in the treatment of IHD and disturbances of cerebral circulation.

The data cited above on the prevalence of IHD in the Armed Forces indicate the ineffectiveness of primary prophylaxis, which should begin in childhood and adolescence. Disturbances in lipid metabolism, vegetative-vascular dystonias, which not infrequently appear in the

first and second decades of life, often precede the disease. However, the organization of prophylactic efforts among schoolchildren and students of the vocational-technical school is a problem for the future. Insufficient attention has been paid to the prevention of IHD among pre-draft age individuals, in the Suvorov or other military training schools. If such prophylaxis is in fact implemented, it has only a general hygiene character, and is not monitored by investigations of lipid metabolism.

The secondary prophylaxis of IHD is also minimally effective. Thus, a decrease in the percentage of the coverage of this category of patients by dispensary-based dynamic supervision has been observed in the Land Forces in the last 5 years, from 84 percent to 79 percent. An increase in the frequency of exacerbations of the illness (from 15 percent to 19 percent) and complications (from 1 percent to 2 percent). When the military districts and groups of troops have been checked, serious deficiencies in the organization of prophylactic efforts have been observed in the Baltic Military District, the Odessa Military District, the Transbaykal Military District, the Ural Military District, the Transcaucasus Military District, and the Central Forces Group. These mainly boil down to an in-depth medical examination which is not always carried out fully, to insufficient monitoring of the nutrition of officers, to the unsatisfactory state of physical training, especially of officers of headquarters and of

non-combattant subdivisions, and to a formalistic attitude toward the fulfillment of medical prophylactic recommendations.

The problem of the prevention of cardiovascular diseases in the Army and Navy is not only a medical one, but a social one as well. It can be solved successfully only with the active participation of the command, of all rear services, and social organizations.

#### Footnotes

1. V. K. Balasevich, *Physical Culture for Each and Every Person*, Moscow, 1988, p 208.
2. A. M. Kalinina, et al., *Kardiologiya*, 1989, No. 6, pp 29-32.
3. N. V. Perova, *Ibid.*, 1989, No. 6, pp 5-9.
4. Z. Sadovskii, et al., *Novosti farmatsii i meditsiny* (Warsaw), 1989, No. 2, pp 34-37.
5. J. A. Ballweg, et al., *Milit. Med.*, 1989, Vol. 154, No. 4, pp 165-168.
6. V. Conner and J. Bristow, *Coronary Heart Disease Prevention*, 1986, pp 215-230.

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UDC 578.832.1/577.213.3

**Construction and Expression in *Escherichia coli* of Influenza Hybrid Hemagglutinin Gene H1/H3**

907C0752A Moscow MOLEKULYARNAYA  
*BIOLOGIYA* in Russian Vol 24 No 2, Mar-Apr 90  
pp 408-416

[Article by V. A. Petrenko, S. M. Kipriyanov, G. A. Mizenko, A. M. Yeroshkin, G. F. Sivolobova, M. Yu. Rukavishnikov, Z. A. Akimenko, A. N. Boldyrev and V. V. Kalashnikov, All-Union Scientific Research Institute of Molecular Biology, "Vektor" Scientific Industrial Association, Koltsovo, Novosibirsk Oblast]

[Abstract] Conventional genetic engineering technology was utilized in the construction and expression of a hybrid influenza virus hemagglutinin (HA) gene, in which a part of the surface epitope of HA H1 was replaced by a homologous H3 sequence. Plasmid pHH13 was constructed from plasmid pUR292 for microbial synthesis in *E. coli* for production of hybrid HA (H1/H3) as a fusion protein with  $\beta$ -galactosidase. The chimeric protein reacted with antibodies specific for H1 and H3 determinants. Additional immunochemical studies demonstrated that the reaction evidently involved antibodies directed against the C-terminal HA domains. Figures 7; references 26: 1 Czech, 13 Russian, 12 Western.

UDC 576.8.097.29

**pH-Dependent Structure and Interaction of Ricin Subunits**

907C0752B Moscow MOLEKULYARNAYA  
*BIOLOGIYA* in Russian Vol 24 No 2, Mar-Apr 90  
pp 431-437

[Article by A. G. Tonevitskiy, S. Yu. Venyaminov\*, T. L. Bushuyeva, N. A. Maysuryan and M. A. Goncharskaya, All-Union Cardiological Scientific Center, USSR Academy of Medical Sciences, Moscow; \*Protein Institute, USSR Academy of Sciences, Pushchino, Moscow Oblast]

[Abstract] Studies were conducted on the effects of pH 4.0 (0.1 M phosphate buffer) and 7.0 (0.1 M sodium acetate buffer) on the structure and interaction of ricin A and B subunits. CD and intrinsic fluorescence spectra demonstrated that once the single disulfide bond between the A and B subunits was broken by dithreitol there was no significant interaction between the subunits at the secondary or tertiary level at pH 7.0. In addition, neither the intact ricin molecule nor the subunits underwent any structural changes as result of the change in pH from 7.0 to 4.0. However, changes in thermostability were noted. Stability of the native molecule increased by 12°C, while that of the A and B subunits was some 25 - 35°C below that of intact ricin. In addition, as the pH decreased the  $K_a$  for the association of A and B subunits increased due to hydrophobic interactions. These observations suggest

that the cytotoxic effects of ricin, which require dissociation of the subunits for ingress into cells, apparently involve organelles with neutral or slightly alkaline pH which would prevent subunit association. Figures 6; references 18: Western.

UDC 575.313

**Cloning and Regulation of Gene Expression of EcoRV Restriction and Modification System**

907C0752C Moscow MOLEKULYARNAYA  
*BIOLOGIYA* in Russian Vol 24 No 2, Mar-Apr 90  
pp 438-447

[Article by A. N. Kravets\*, M. V. Zakharova, A. S. Solonin, N. P. Kuzmin, V. I. Tanyashin, L. I. Glatman\*\*, A. F. Moroz\*\* and A. A. Bayev, Institute of Biochemistry and Physiology of Microorganisms, USSR Academy of Sciences, Pushchino, Moscow Oblast; \*Kiev Scientific Research Institute of Epidemiology and Infectious diseases imeni L. V. Gromashevskiy, Ukrainian SSR Ministry of Health; \*\*Scientific Research Institute of Epidemiology and Microbiology imeni N. F. Gamaleya, USST Academy of Medical Sciences, Moscow]

[Abstract] A series of recombinant plasmids belonging to different compatibility groups were engineered to bear EcoRV restriction and methylase functions. Expression in *E. coli* of vector pVE8 demonstrated that the promoter was comparable in efficiency with phage  $\lambda$  early promoter and operated at 70 percent efficiency of  $\lambda$   $P_1$  promoter. Efficiency of the methylase gene promoter was two-fold lower than that of the restriction promoter. In addition, in cases in which EcoRV was under the additional control of phage  $\lambda P_R$  promoter a 30- to 40-fold increase in restriction synthesis was observed in conjunction with inactivation of the temperature sensitive repressor of phage  $\lambda$ -c1857. In the latter cases production of EcoRV restriction amounted to ca. 10 percent of the total cell protein. Figures 3; tables 3; references 39: 13 Russian, 26 Western.

UDC 577.323.435

**"Samson" Software Package for Analysis of Primary Structure of Biopolymers**

907C0752D Moscow MOLEKULYARNAYA  
*BIOLOGIYA* in Russian Vol 24 No 2, Mar-Apr 90  
pp 524-529

[Article by S. Ye. Vernoslov, A. S. Kondrashov, M. A. Roytberg, S. A. Shabalina, O. V. Yuryeva and N. N. Nazipova, Scientific Research Computer Center, USSR Academy of Sciences, Pushchino, Moscow Oblast]

[Abstract] Cursory description is provided of a software package intended for analysis of the primary structure of biopolymers, with full description available under the same title by S. Ye. Vernoslov et al. as Nos. 1 & 2, Pushchino, ONTI NTsBI [expansion unknown], 1989.

The software, consisting of 20 application programs, is designed for power users in molecular biology interested in theoretical sequence analysis. The applications are divided into six categories dealing with manipulation of the basic data, estimation of the various sequence characteristics, identification of sequences with defined characteristics, modeling of various molecular processes, sequence comparison, and specialized applications, such as search for distorted sequences in DNA. References 9: 5 Russian, 4 Western.

UDC 577.113.4

### Use of Filamentous M13 Bacteriophage in Protein Engineering

907C0752E Moscow MOLEKULYARNAYA BIOLOGIYA in Russian Vol 24 No 2, Mar-Apr 90 pp 530-535

[Article by A. A. Ilyichev, O. O. Minenkova, S. I. Tatkov, N. N. Karpyshev, A. M. Yeroshkin, V. I. Ofitserov, Z. A. Akimenko, V. A. Petrenko and L. S. Sandakhchiyev,

Scientific Research Engineering Institute of Biologically Active Substances, "Vektor" Scientific Industrial Association, Berdsk, Novosibirsk Oblast]

[Abstract] An analysis was conducted on the application of phage M13 in protein engineering, with the primary view of creating artificial immunogens (vaccines) in the form of M13 bearing a foreign epitope on its surface. Initial steps consisted of construction of ampicillin-resistant M13B by insertion of a fragment of plasmid pBR327 DNA, containing  $\beta$ -lactamase gene, into poly-linker region of phage M13mp10. M13B, in addition, has a BamHI site in gene III which encodes the envelope B protein. Introduction of a synthetic DNA segment coding for a model peptide into the BamHI site resulted in the appearance of the model peptide on the N-terminal terminus of the B protein. Introduction of the foreign peptide into the envelope yielded viable M13 phages with diminished infectivity for *E. coli*, demonstrating that this approach to engineering of vaccines is quite promising. Figures 3; references 19: 7 Russian, 12 Western.

UDC 615.214.31:547.743.1].015.4

**Biotransformation of  
1-thiocarbamoylmethylpyrrolidinethione-2**

907C0812A Moscow

*KHIMIKO-FARMATSEVTICHESKIY ZHURNAL*  
in Russian Vol 24 No 4, Apr 90 pp 7-11

[Article by Ye. F. Kuleshova, A. V. Kadushkin, O. S. Anisimova et al.; VNIKhFI imeni S. Ordzhonikidze, Moscow]

[Abstract] A study of the structure of products of metabolism of dithio-derivatives of pyracetam, 1-thiocarbamoylmethylpyrrolidine-thione-2 (TP), which possesses high antihypoxic and nootropic activity and synthesis and study of the biotransformation of TP were described and discussed. Pyracetam is not metabolized in the organism and is voided in the urine unchanged. The presence in TP of 2 thioamide groups suggested the probability of biotransformation in this case, possibly associated with hydrolytic and oxidative processes which affect C=S groupings. TP metabolism in rats, rabbits and dogs was studied by the method of mass spectrometry combined with TSKh (thiosemicarbazide) and also nuclear magnetic resonance <sup>1</sup>H-spectroscopy with urine collected over 24 hours from the moment of per os administration of the drug. Biotransformation of TP proceeded in two basic directions—by means of sulfoxidation with subsequent replacement of thioxogroups by oxogroups right up to formation of pyracetam and by intramolecular cyclization accompanied by separation of hydrogen sulfide with formation and further transformation of derivatives of 5,6-dihydro-7H-pyrrolo[1,2-a] imidazole. Dehydration of amide or thioamide groups

occurred in some cases with formation of corresponding nitrils. Pharmacological study of the metabolites synthesized showed that some of them display antihypoxic activity not exceeding the activity of TP. References 11: 9 Russian, 2 Western.

UDC 547.466:547.783

**Nootropic Activity of Ureido Acids and  
Thiohydantoin Derivatives**

907C0812B Moscow

*KHIMIKO-FARMATSEVTICHESKIY ZHURNAL*  
in Russian Vol 24 No 4, Apr 90 pp 32-35

[Article by T. V. Golovko, V. A. Parshin, V. V. Asnina et al.; VNIKhFI imeni S. Ordzhonikidze, Moscow]

[Abstract] A study of nootropic properties of ureido acids and cyclic thioureido acids and thiohydantoins and some derivatives prepared by condensation of these compounds with acetals of acid amides involved experiments on 18 - 20 g male mice to determine the effect on the hypoxic state, the convulsive effect of thiosemicarbazide and corazole and the duration of the latent period of the conditioned reaction of passive avoidance. N-thiocarbamoylglycine showed relatively pronounced antihypoxic properties; ureido acids Ia and Id produced an anticonvulsive effect on a model of gamma-amino butyric acid-deficit spasms. 2-thiohydantoin displayed a pronounced antagonism to corazole. Ureido acid Ib extended the duration of the latent period of the conditioned reaction of passive avoidance. All preparations equalled pyracetam in effectiveness. All possessed nootropic activity. References 9: 2 Russian, 7 Western.

UDC 795.3

**Management of Neurotic Reactions in Cats by  $\beta$ -Endorphin Conjugate**

907C0733C Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 311 No 6, Apr 90 pp 1500-1505

[Article by A. I. Karamyan, corresponding member, USSR Acad. Sci., Yu. A. Pankov, full member, USSR Acad. Med. Sci., T. N. Sollertinskaya, A. L. Protsenko and I. L. Kofman, Institute of Evolutionary Physiology and Biochemistry imeni I. M. Sechenov, USSR Academy of Sciences, Leningrad; Institute of Experimental Endocrinology and Endocrine Chemistry, USSR Academy of Medical Sciences, Moscow]

[Abstract] Immunization with  $\beta$ -endorphin has been shown to alleviate neurotic behavior in monkeys and hedgehogs, with the change in behavior correlating with maximum antibody titer. Accordingly, analogous studies were conducted on male cats to assess the effects of immunization with  $\beta$ -endorphin-BSA (bovine serum albumin) conjugate in Freund's complete adjuvant in order to expand the scope of species-related information. Neurotic behavior was induced to interfere with conditioned food reflex, then the cats were twice injected subcutaneously, with 250 - 300  $\mu$ g/kg of  $\beta$ -endorphin ten days apart (dosage employed in primates and hedgehogs) or with 150  $\mu$ g/kg of  $\beta$ -endorphin at 10- or 20-day intervals. The response to 250 - 300  $\mu$ g of  $\beta$ -endorphin was biphasic: gradual recovery of the conditioned food response over 1 - 3 days, and complete alleviation of neurotic behavior over the 5 - 20 days following injection. With the smaller dose and the longer interval between immunizations, the behavioral improvement, in the form of normal performance on conditioned response test, persisted for 40 - 50 days, whereas with the higher dose improvement lasted for only 20 - 30 days. In addition,  $\beta$ -endorphin was found to be of greater benefit in animals with an aggressive form of neurosis and had a calming effect; while in cats with languid manifestations of neurosis  $\beta$ -endorphin exerted a stimulant action. Figures 3; references 15: 9 Russian, 6 Western.

UDC 612.81

**Interhemispheric EEG Asymmetry and Negative Emotional Stimuli**

907C0751A Moscow FIZIOLOGIYA CHELOVEKA in Russian Vol 16 No 2, Mar-Apr 90 pp 22-30

[Article by V. F. Konovalov and I. S. Serikov, Institute of Biological Physics, USSR Academy of Sciences, Pushchino]

[Abstract] An analysis was conducted to determine correlation parameters between asymmetry of  $\alpha$  and  $\theta$  patterns on EEG and negative stimuli in 13 right-handed males, 25 - 35 years old. The test system involved

presentation of neutral and negative (80 V electric stimulus to finger) verbal stimuli with concomitant assessment of occipital and temporal EEG asymmetry. Baseline studies demonstrated a positive coefficient of asymmetry of the occipital  $\alpha$  waves in 77 percent of the subjects, i.e., the  $\alpha$  energetic profile was dominant in the right hemisphere, and 23 percent presented with negative coefficient indicative of left hemisphere predominance. In the case of temporal recordings, a positive coefficient of asymmetry was observed in 46 percent of the subjects. Analysis of  $\theta$  occipital and temporal recordings showed that positive coefficients of asymmetry prevailed in 92 percent and 100 percent of the subjects, respectively. Emotional stress was found to induce three types of change in EEG asymmetry: One type consisted of positive coefficients of asymmetry in the occipital regions in some subjects and in the temporal region in others; the second type involved negative occipital and temporal coefficients; and finally, the third type consisted of a mixed-type response characterized by equivalent positive and negative asymmetry of occipital and temporal  $\alpha$  waves. Changes in the  $\alpha$  and  $\theta$  waves were greater in the occipital than in the temporal recordings, with changes in  $\alpha$  exceeding changes in  $\theta$ . The higher information content of the  $\alpha$  waves was evidently due to their dominance in the brain wave spectrum, greater uniformity and correlation with the degree of activation of subcortical formations. In addition, the results indicate that EEG asymmetry may be used to assess the effects of negative emotional stress. Figures 4; references 32: 28 Russian, 4 Western.

UDC [612.014.421-073.97:612.82]:681.3

**Comparison of Expert and Automatic EEG Classification**

907C0751B Moscow FIZIOLOGIYA CHELOVEKA in Russian Vol 16 No 2, Mar-Apr 90 pp 31-40

[Article by Ye. A. Zhirmunskaya and I. I. Goncharova, All-Union Scientific Research Institute of Technical Esthetics, Moscow]

[Abstract] A comparison was conducted on EEG pattern classification based on expert opinion and results of computer processing. The EEG recordings were obtained from 98 clinically healthy men and women ranging in age from 25 - 46 years. The cohort consisted of 74 right-handed, 11 left-handed, and 13 ambidextrous individuals. Factor analysis of 15 EEG physiological groups and correlation with automatic spectrum analysis revealed that expert classification is based not only on subjective interpretations, but is also supported by unambiguous objective criteria. Accordingly, the findings indicate that computer-based probability-density approach to EEG pattern classification constitutes a reliable and rapid aid to EEG interpretation. Figures 3; tables 2; references 12: 6 Russian, 6 Western.

UDC 612.821:616.891

**Functional Enhancement of Visual Analyzer in Healthy Subjects by ACTH<sub>4-10</sub>**

907C0751C Moscow FIZIOLOGIYA CHELOVEKA  
in Russian Vol 16 No 2, Mar-Apr 90 pp 151-154

[Article by V. V. Kolbanov, V. V. Nakorchemnyy, A. A. Nevezorov, V. N. Nezavibatko, M. A. Ponomareva-Stepnaya, L. Yu. Alfeyeva and V. N. Potaman, Military Medical Academy imeni S. M. Kirov, Leningrad]

[Abstract] The effects of ACTH<sub>4-10</sub> (Met-Glu-His-Phe-Pro-Gly-Pro) on visual function were investigated on the authors at weekly intervals following intranasal instillation of 400 - 500 µg/person of the peptide in a double-blind study. Testing conducted 40 - 50 min after instillation demonstrate that in each case there was noticeable improvement in light sensitivity, color perception and functional flexibility. The changes could not be attributed to any subjective factors or inadvertent training, but seemed to be correlated with the generally acknowledged improvement in CNS function induced by ACTH fragments. Tabls 2; references 14: 11 Russian, 3 Western.

## Dynamic Features and Territorial Differentiation of Infant Mortality in Latvia

907C06884 Riga IZVESTIYA AKADEMII NAUK LATVYSKOY SSR in Russian No 5, May 90 pp 84-89

[Article by Z. Klintaya, Latvian University]

**[Text]** Health, the foundation of which is laid from birth, is a prerequisite for an active life. Unfortunately, the statistics do not provide dependable indicators of the health of people in different stages of their life. It may be assumed, however, that the health of infants correlates with infant mortality indicators in the same territories and among the same population groups. Therefore, infant mortality trends can serve as an indirect characteristic of health. With this purpose in mind, we conducted a detailed analysis of the dynamics of infant mortality and its territorial differentiation in the Latvian SSR.

Infant mortality in the Latvian SSR exhibited a tendency to decline in the last 20 years, especially since the second half of the 1970s, and in 1988 it attained 10.8 percent.<sup>1</sup> It is evident from Figure 1 that the curve characterizing infant mortality from 1970 to 1987 reached its maximum of 20.5 percent in 1975, such that an almost two-fold decline occurred subsequently. In the USSR as a whole, beginning in the 1980's these indicators stabilized at a level of 25-26 per thousand (25.4 per thousand in 1987),<sup>2</sup> in contrast to the Latvian SSR, which had the lowest indicators among the union republics. Nonetheless in comparison with developed European countries, infant mortality remains relatively high

in our republic; for example, in 1987 it was 8.3 per thousand in the FRG, 5.7 per thousand in Sweden and 6.8 per thousand in Switzerland.<sup>3</sup>

Differences in infant mortality exist in the republic between cities and rural areas, although the difference between the indicators is only an average of 1-2 percent—that is, infant mortality is an average of 10-15 percent higher in rural areas than in cities. This is chiefly the result of lower availability of medical care. However, fluctuations in the curves for rural areas and cities in 1970-1986 practically coincide (see Figure 1), and in view of a sharper decline in the indicators for rural areas, the curves converge.

If we analyze the dynamics behind changes in mortality indicators (assuming the 1970 level to be 100), we find that in the indicated period they decreased more dramatically in rural areas—74.3, while in cities they decreased only down to 86.7; in rural areas, these indicators are correspondingly lower than the republic average (81.2). Differences in infant mortality between individual cities and rural rayons exceed the difference between indicators for cities and rural areas in general. Typically the indicators for the decline in infant mortality in republic-subordinated cities (95.2), including Riga (92), exceed the republic average. This is indirect evidence of the effect of specific environmental aspects. Such differentiation is also observed among different rayons of the republic, which we will describe in greater detail.

A map (Figure 2) was compiled from the results of analyzing territorial differences in the average indicators of infant mortality in the last 16 years. The highest indicators are typical of rayons in eastern Latvia—Daugavpilskiy, Kraslavskiy and Rezeknenskiy. This

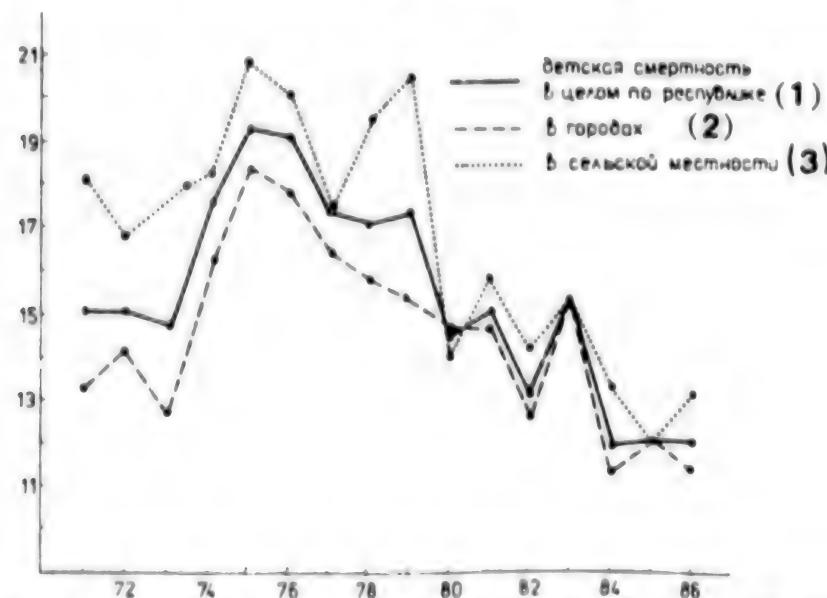


Figure 1. Dynamics of Infant Mortality in the Latvian SSR in 1971-1987 (Compiled by the author from reports of the Latvian SSR State Statistical Committee for the corresponding years, and from *Naseleniye SSSR Statisticheskii zhurnal* (The USSR Population. Statistical Collection), Moscow, Finansy i statistika, 1988, p 345).

Key: 1. Infant mortality in the republic as a whole. 2. In cities. 3. In rural areas.



Figure 2. Infant Mortality in the Latvian SSR in 1971-1986

Key: 1. Infant mortality; 2. Above the republic average; 3. High; 4. Elevated; 5. Below the republic average; 6. Reduced; 7. Low; 8. Very low.

elevated level of infant mortality can be explained in part by relatively poor development of sanitation and hygiene, a smaller number of physicians and medical personnel than the republic average, and the relatively poorer development of the social infrastructure as a whole. A relatively high level of infant mortality also occurs in cities and rayons in central Latvia, although medical services are more accessible. Ecologically unfavorable cities—Riga, Jurmala, and Olayne—and the denser network of highways and railroads are located here. On the average, in the last 16 years, this indicator for the republic's capital, Riga, exceeds both the city average and the republic average, which is an indication that the ecological situation is deteriorating—that is, that the environment of the large city is beginning to affect the health of its population unfavorably.

In western Latvia the level of infant mortality is relatively low, except in Liyepayskiy and Saldusskiy rayons.

If we follow the dynamics of infant mortality differentiated territorially in 1971-1986, we can assert that in eastern rayons of Latvia (except in Daugavpils and Rezekne), its level has remained high, though on a republic average a tendency for infant mortality to decline is observed.

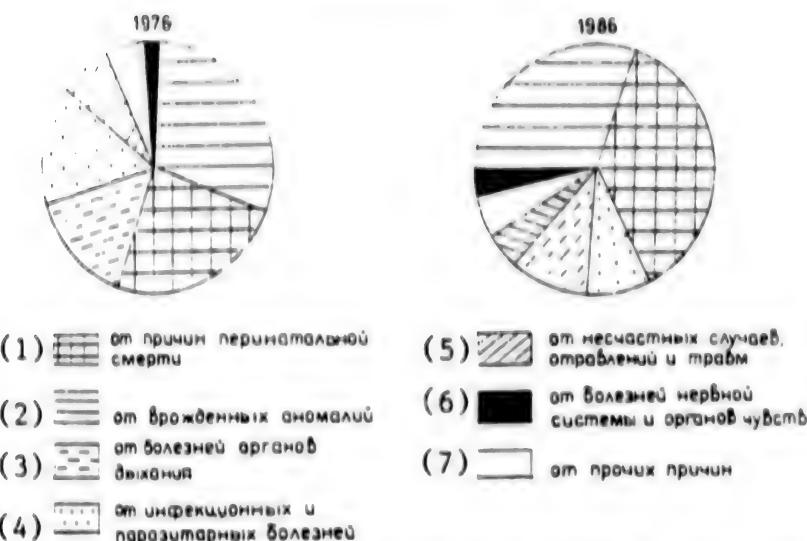
A trend opposite to the average republic trend revealed itself in recent years in western Latvia—growth of infant mortality. Such a difference cannot be explained by the age structure of mothers (see Table), which is not changing so abruptly. In our opinion, one of the reasons

for this unexpected growth of infant mortality is the worsening of the ecological situation in the republic. Ecologically unfavorable conditions often manifest themselves indirectly. Geographical factors, for example location and climate (prevailing winds, precipitation etc.), play a certain role in this. The following example can be cited as confirmation of this: Ventspils is on the shore of the Baltic Sea, owing to which it enjoys better aeration than Daugavpils (in southeastern Latvia), which is located in a low point of the Daugava River valley. Both cities contain chemical enterprises (though of different profiles), and their vicinities are suffering from pollution, but in Ventspils the pollution is somewhat compensated by natural conditions.

A polluted environment also has a stressful influence upon the individual's mind and his way of life owing to his awareness of impending ecological danger. However, the influence of this factor on overall health has been studied little thus far.

Of course, ecological factors are not the only ones that influence infant mortality. Professor M. S. Bednyy distinguishes the following medical-demographic groups of factors which also affect the level, nature and differentiation of infant mortality. Factors of the first group have to do with "infant-society" interaction, the second group of factors involve the relationship to the infant in the family, and the third group includes endogenous factors, including hereditary factors, the course of pregnancy and so on.<sup>4</sup>

The relationship that different factors have in their influence on the level and dynamics of infant mortality



**Figure 3. Structure of the Causes of Infant Mortality in the Latvian SSR in 1976 and 1986**

Key: 1. Due to causes of perinatal death; 2. Due to congenital abnormalities; 3. Due to respiratory diseases; 4. Due to infections and parasitic diseases; 5. Due to accidents, poisonings and injuries; 6. Due to diseases of the nervous system and sensory organs; 7. Due to other causes

may be assessed from the structure of the causes of infant mortality and its variations (Figure 3).

The probability of the death of infants in the first year of their life varies in the course of this entire time interval. It is highest during the first month of life, especially in the first days and the first week of life. In the first week of life the infant's health is determined chiefly by prenatal endogenous factors. Infant mortality following the first month of life depends, in contrast to the first weeks, more on exogenous factors: on the environmental conditions which it encounters, including the care it receives.<sup>5</sup>

Two basic groups clearly dominate the structure of the causes of infant mortality in the Latvian SSR in recent years: mortality in early childhood (37.5 percent of all causes in 1986) and congenital abnormalities (30.5 percent). Infectious and parasitic diseases occupy third place in the overall structure of the causes of infant mortality.<sup>6</sup>

Beginning in the 1970's, the proportion of congenital abnormalities gradually increases in the structure of the causes of infant mortality. Territorial differences exist in relation to this indicator, as well as in relation to the general indicators of infant mortality, but if we compare the two indicators for 1971-1986, we can isolate rayons and cities in which the levels of these indicators correlate (Figure 2 and Figure 4).

In both cases an elevated level is typical of two rayons in eastern Latvia, Daugavpilsskiy and Kraslavskiy, and of Gulbenkiy Rayon in northeastern Latvia. It should be explained in regard to Daugavpilsskiy Rayon that high indicators are the result of the presence of the republic

psychoneurological children's hospital in Kalkun, and the number of infants that had died there are added to the number of deceased infants born in the rayon, while the infant mortality factor is calculated per thousand infants born in this rayon. Abnormal values are the result.

The next zone to be distinguished is one of relatively high indicators (exceeding the republic average) in the republic's center, which includes the cities of Riga, Jurmala and Jelgava, and the rayons contiguous to them. In western Latvia, an elevated level is typical only of Liyepayskiy Rayon in both cases. We can distinguish a group of rayons in the western coast of Latvia, besides the above-mentioned Liyepayskiy, Ventspilsskiy, Talsinskii and Kuldigskiy rayons, in which the overall average infant mortality indicators are not only below the republic average but also the lowest in Latvia.

A special situation has evolved in the port city of Ventspils—this is one of the ecologically dangerous cities in which ammonium, methanol and other dangerous chemicals are stored and transferred, and mineral fertilizers (potassium salts) are transloaded at the port. Infant mortality due to congenital abnormalities was among the lowest on the average in the period from 1970-1986 in Ventspils. This can be explained by the fact that ecologically harmful enterprises manifest their influence differently—for example as an increase in the incidence of Down's syndrome among infants.<sup>7</sup> It should also be noted that the prevailing winds carry some of the pollutants to nearby territories. However, if we trace the dynamics of infant mortality indicators pertaining to young infants beginning in the 1970s, a tendency toward growth manifests itself in Ventspils and Ventspilsskiy Rayon. This tendency contradicts the republic trend—



**Figure 4. Infant Mortality Due to Congenital Abnormalities in the Latvian SSR in 1971-1986**

Key: 1. Infant mortality due to congenital abnormalities; 2. Above the republic average; 3. Very high; 4. High; 5. Elevated; 6. Below the republic average; 7. Reduced; 8. Low; 9. Very low.

the reduction of this indicator. This situation is also observed in the dynamics of mortality due to congenital abnormalities.

Perinatal mortality and corresponding causes of death have dominated the structure of infant mortality in recent years. Although its absolute level is decreasing (4.9 percent in 1986)<sup>8</sup>, its proportion within the overall structure of the causes of death is increasing. If we analyze the dynamics behind early infant mortality, we can assert that the tendency for this indicator to decline is determined by a decrease in its level in the largest city, Riga, in which we find the largest proportion of deceased infants, as well as in Jurmala, Liepaja, Rezekne and Jelgava. It should be noted that differences in overall infant mortality indicators have been observed rather distinctly between rural areas and cities, especially large ones (Daugavpils and Liepaja) (Figure 2), while differences in early infant mortality are less significant, since primarily endogenous factors influence it. And territorial differences in overall infant mortality are the result of differences in exogenous factors, the characteristics of which have yet to be clarified.

Another factor influencing infant mortality is the mother's age. If we compare the age structure of mothers of all infants born and mothers of deceased infants (see table), we can observe a certain pattern: The older the mother, the relatively greater the probability of losing a child. Evidence of this can also be found in another factor influencing infant mortality—the order of the deceased child's birth. Comparing the structure of the

order of birth and of deceased infants, we can observe the greatest inconsistencies in relation to the first child (0.86) and the fourth and fifth children (respectively 0.74 and 0.85). The first and fifth children have a relatively greater probability of dying than the second and third. And this is understandable: The fourth and fifth children are usually born to mothers 30 or more years old. Therefore, the probability of dying depending on the order of birth correlates with the mother's age.

#### Ratio of Born and Deceased Infants With Respect to Order of Birth and Age of Mother in the Latvian SSR in 1987\*

Order of Child's Birth	Ratio of Born to Deceased Infants	Mother's Age, Years	Ratio of Born to Deceased Infants
First	0.86	Under 20	1.29
Second	1.46	20-24	1.02
Third	1.11	25-29	1.04
Fourth	0.74	30-34	0.87
Fifth and higher	0.85	40 and older	0.63

\*Calculated by the author on the basis of current report data

It may be concluded from the data examined above that the trend observed in growth of the proportion of families with two and three children and concentration of births primarily among mothers 20 - 29 years old can promote a further decline in infant mortality, if other factors do not cause it to rise.

In the 1980s the number of children in the republic born to mothers out of wedlock has been increasing (the proportion of the total number of children born in 1980 was 12.4 percent, while in 1986 it was as much as 15.04 percent).<sup>9</sup> According to our research the proportion of infants in eastern Latvia dying prior to an age of one year and born to unmarried mothers varies in individual years by approximately 10 - 20 percent, while the proportion of such infants within the overall structure remained practically unchanged. Consequently this circumstance does not play a significant role in the dynamics of infant mortality.

Analyzing territorial differentiation and the dynamics of infant mortality in the Latvian SSR, we can see that the pattern assumes a rather complicated mosaic that cannot always be explained by the action of known factors, including ecological ones. When rayons are revealed to be abnormal at the present level of research, if we wish to specify which infant mortality factors dominate and if we wish to obtain a possibility for predicting changes in infant mortality in relation to the age composition of mothers and the state of the environment, we would need additional information and special research.

#### Footnotes

1. CINA, 4 February 1989.
2. *Naseleniye SSSR, 1987: Statistich. sb.* (USSR Population, 1987: Statistical Collection), Finansy i statistika, Moscow, 1988, p 344.
3. POPULATION SOCIETES: BULLETIN MENSUEL D'INFORMATIONS DEMOGRAPHIQUES, ECONOMIQUES, SOCIALES, October 1988.
4. M. S. Bedny, *Demograficheskiye faktory zdorovya* (Demographic Factors of Health), Finansy i statistika, Moscow, 1988, p 236.
5. R. Ignatyeva, "Infant mortality: Status, Trends, Prospects," *NARODONASELENIYE. NASHE ZDOROVYE*, No 43, 1982, pp 17-18.
6. Calculated on the basis of *Naseleniye SSSR, 1987*, p 405.
7. CINA, 22 March 1989.
8. *Naseleniye SSSR, 1987*, p 348.
9. *Naseleniye SSSR, 1987*, p 217.

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#### Radiation Medicine Center to Open in Bryansk

907C0710C Moscow SELSKAYA ZHIZN in Russian 12 May 90 p 2

[Article: "Radiological Center", Unattributed.]

[Text] Foreign currency worth 40 million rubles was allocated from the union budget for the construction and

equipment of a republic center for radiological medicine in Bryansk. Another 20 million rubles has been allocated for construction of social, cultural and consumer service facilities.

A foreign company has been approached to carry out this work. The center, which is to be fully completed in 1993, will meet world standards.

The complex will include a 350 bed hospital and a polyclinic capable of handling 600 visits per shift. Over 50 motor vehicles will convey people here for examinations from rayons subjected to radioactive contamination as a result of the Chernobyl Nuclear Power Plant accident. They will be accommodated in a boarding hotel with a capacity of 300 guests.

Four hundred fifty thousand persons reside in Bryansk Oblast on contaminated territory, and another 200,000 live in neighboring oblasts—Kaluga, Tula, Orel and Smolensk.

UDC 614.25(47+57)

#### Several Aspects of the Use of Insurance Medicine Principles in the USSR

907C07604 Moscow SOVETSKOYE ZDRAVOOKHRANENIYE in Russian No 6, Jun 90 pp 3-7

[Article by O. P. Shchepin, V. V. Grishin, and V. Yu. Semenov, All-Union Research Institute of Social Hygiene, Economics, and Administration of Public Health imeni Semashko, USSR Ministry of Health, Moscow]

[Text] In the past 20 - 25 years of the development of public health in our country, an aggravation of a complex of issues connected with its financial support has become evident. Prior to this time, the shortage of funds allocated by the government for the public health was not felt so acutely. Moreover, the achievements of our country in the organization and implementation of measures for prevention and elimination of diseases were a model for many countries. The strategy chosen and the forms of work during the period when epidemic, parasitic, social, and especially dangerous diseases were being eliminated and extensive sanitary measures were being implemented made it possible to achieve excellent results in improving the health indices of the population and increasing their life span at relatively modest expense.

However, the easily eliminated illnesses were replaced by diseases and conditions whose causes are primarily hereditary factors—unhealthy habits, unbalanced nutrition, and unfavorable ecological conditions, which are having increasing influence on the morbidity, the mortality, and (thus) the anticipated life span. All of this requires not only new approaches to medical measures,

but also changes in the planning, financing, organization, and coordination of the work of all public health services and institutions with other sectors of the economy and monitoring their activities. It is necessary to find new methods of stimulating the activity of the ministries and government agencies in protecting the health of the population, as well as the citizens in preserving and fortifying their own health.

In order to handle the many problems that have arisen, as valuable as medical programs, the state should efficiently search for ways and means of allocation and attraction of resources, especially financial ones. However, the changing situation has not been adequately assessed in our country. Moreover, the lingering principle of financing the sectors of the social and cultural complex, including public health, has brought "...the social sphere to a state of neglect and even partial degradation. We are now feeling directly how the attitude to the social sphere was another of the factors of stagnation, a cause of rising social tension, the fruit of which we are harvesting today."<sup>1</sup>

It should be pointed out that the investments of financial resources in the sector grew continually in absolute terms, while, until recently, the percentage of outlays of the state budget on public health dwindled. At the same time, the available resources are not being used wisely, the techniques of the therapeutic and diagnostic processes are not state of the art, and the prospects for an outpatient or polyclinic component in the provision of medical care to the population are clearly inadequate. The public health policy currently practiced has meant that most of the quality medical services are provided in the hospitals. The poor condition of the outpatient and polyclinic facilities is the reason why patients enter the hospital without being sufficiently prepared for hospitalization and their examination in the hospital is long and drawn out. Nor is there an economic incentive for the fastest possible treatment, either for the patients themselves or for the hospital personnel. As a result, every fourth inhabitant of the country is hospitalized an average of 16 days a year, which is much larger than the figure for the economically advanced countries. All of this leads to an unreasonable increase in costs of providing various services and more expensive medical care.

The deficiencies that exist are largely due to the current mechanism of funding, based on the available beds, polyclinics, staff, etc., as well as the rigid standardization of both the rights and duties of the practicing staff and the administration of the public health agencies and facilities.

The critical condition in which Soviet public health found itself demanded emergency measures. For the first time in many years, substantial additional funds were allocated to public health—to increase the salaries of the medical workers, 3.6 billion rubles (although the implementation of this measure dragged on for 6 years, as a result of which the salaries of the physicians continue to

remain behind the average worker of the USSR and this gap is continuing to increase); for priority measures to strengthen the logistical base of the sector, 5.4 billion rubles; additional foreign exchange was also made available to purchase medicine.

Much has been written on the public health agencies and facilities. In addition to critical comments, these publications also contain proposals for improvement, generally calling for a better quality of medical care. It is not clear what they have in mind: a higher level of training of the medical personnel; more efficient use of the methods of prevention, diagnostics, and therapy; improved stocks of medical drugs and equipment; the need for immediate strengthening of the logistical base and improved funding of the sector; or something else altogether.

However, while mentioning the shortage of funds allocated from the state budget on public health, all too often they merely list the possible sources of monetary resources, the main share going to the resources of the enterprises and the economic organizations. At the same time, in our opinion, much too little attention is given to analysis of the current system of financing, evaluation of the production and financial-economic activity of the subdivisions of the sector, the methods of rational and effective utilization of the existing personnel, technical and financial potential, and the selection of therapeutic and diagnostic measures and technologies from the standpoint of their economic effectiveness and achievement of the best results in providing medical and sanitary preventive care to the population and in improving their health indices. Almost no work has been done on the identification and possible elimination of the reasons for the poor development of sectors that are associated with public health, such as those that produce medication, medical items, equipment, apparatus, appliances, and the various devices that are essential to the proper functioning of the health care services.

At present, in keeping with the environment of the new economic mechanism in the country, a change in the funding of public health is taking place. On the territorial level, allocations are now paid out per inhabitant, and the public health facilities will receive funds per unit volume of activity: hospitals, per patient treated; polyclinics, per inhabitant in their district; the emergency medical care service, per call; and so forth. These standards will also be used for mutual accounting between facilities. The managers and personnel of the facilities will have ample authority in the use of the funds received.

At the same time, the prevailing principle of funding the public health from the state budget alone does not ensure that the optimal volume of funds will be devoted to these goals. The position is complicated by the fact that, in recent years, the rate of growth in the remuneration of labor has outdistanced the rate of growth of the labor productivity. On the whole, this was to be expected since there has come into being in our country an unnatural situation (in our opinion) where the remuneration of

labor amounts to no more than 35 - 40 percent of the national income. But increasing the proportion of remuneration of labor results in a decreasing of the proportion and, thus, the total of the funds earmarked for the nonproduction sphere. Consequently, there is no reason to hope for substantial improvement in the position of public health. The conflicts between the existing mechanism of funding and the demands of the population for medical care are becoming even more intense.

In the current publications, one is apprehensive of the ease with which a number of authors move from recent approbation to sharp criticism or even total denial of the effectiveness of socialized public health, the role of the government in solving problems of public health, the centralized allocation of funding, and the planned development of the infrastructure and the training of personnel. Some of them are campaigning for an immediate adoption of a medical insurance system in the country.

Unfortunately, there are no publications with specific proposals for implementation of the principles of insured medicine in our country. All that there is are general proposals and some analysis of the historical and Western experience. This experience testifies that insured medicine is not a panacea for all problems of public health, and a sober analysis of its possibilities will allow us to avoid a whole series of added difficulties that may arise unless provision is made for their possible impact while working out the concept for utilization of elements of insured medicine as apply to our country. Obviously, a system of health insurance is only possible with a radical change in the tax structure of the country.

Furthermore, the growing processes of economic independence of the union republics and the different levels of their economic and social development give reason to declare that a single insurance program cannot exist in the country. Consequently, determination of the range of mandatory (guaranteed) and optional services may be done in a decentralized way, depending on the availability of personnel, the logistical base, and the level of development of the particular services. In an economically prosperous republic, territory, or oblast, the insurance premiums may provide for various therapeutic and diagnostic measures, medical and social assistance, and even partial compensation for availing oneself of pay services. In another region, the insurance funds may only cover outpatient services or hospital treatment and purchase of medication and of medical equipment.

All of this, in the final analysis, may bring about inequality in reception of medical care among the citizens. The Western experience testifies that the urban population has the advantage, the winners are those among the blue collar and white collar employees of nonprofit enterprises and organizations and those of promising sectors of the economy.

A thorough discussion is necessary for the selection of the principle of insurance—voluntary or mandatory. If the insurance is not mandatory, it may be expected that

the young and most able-bodied workers, whose health is in a satisfactory condition, will refuse to become insured. As a result, the volume of insurance funds will be rather modest. It is also important to determine the form of insurance—state, private, mixed—each of these having its own path of development, its own advantages and drawbacks. Thus, if it is decided on a private insurance with differing amount of insurance premium, the history that is now taking place with the cooperatives may be repeated: the unregulated creation of insurance agencies (and the cooperatives themselves may act as such) will make social and medical supervision and gathering of economic and statistical information difficult and create an environment ripe for abuse and scheming.

The adoption of a medical insurance system requires the creation of an insurance institution: Changes in the tax liability and legislation, creation of insurance offices, formation and training of the personnel of these offices, etc. Obviously, this work will take some time to be accomplished, as well as a certain amount of expenditure on training of various specialists and circulation of documents; it will be necessary to change the management structure of the sector and the function of the public health bodies.

With medical insurance, the primary organizational links (regional and municipal) will bear the main load. But how can this be reconciled with the present closing down of regional public health departments in the cities? Will it be necessary to reopen these bodies at a later date, expanding their functions, or will this work be placed on the shoulders of the territorial medical associations?

Since one of the basic conditions of medical insurance is strict compliance with the obligations assumed with respect to the insured parties, it may happen that they will demand a higher quality of medical care, use of modern methods of diagnostics and treatment of diseases, and consultations with highly trained specialists. It should also be noted that therapeutic measures generally prevail over preventive ones in a medical insurance system.

The above points are sufficient for a sober consideration of the feasibility of replacing the government public health system by a fundamentally different system, based on health insurance, in a short space of time. It is right to be skeptical: if today we are not able to sort out the cluster of organizational, financial, economic, logistical, and other problems and ensure a rational and effective utilization of the available resources, it will hardly be possible to do so by adopting a more complex system of medical insurance without a preliminary training of the physicians to function in the new economic conditions.

In our estimation, a gradual creation of health insurance services may be done as a supplement to the existing system of public health in the form of an agency that supervises the income of additional revenue and its utilization for funding of the public health.

The different economic conditions, the spread of self management, and the changes in the rights of owning the means of production are radically changing the attitude of the workers (both in their collectivity and each individual) to their state of health. The adoption of cost accounting, leasing, and cooperative relationships in the economy will serve as the basis for encouraging the labor collectives to intensify their activity, increase the volume of product produced, and (thus) increase the revenues of the enterprises. And this is only possible if the workers are healthy and are able to work properly.

On the other hand, the events of recent history show that the population is deeply dissatisfied with the state of the social sphere and the development of its infrastructure, including public health. For example, one of the demands of the striking miners was improved medical care. And the labor collectives are willing to invest further resources in the development of the sector.

Finally, the Law of the USSR "On the state enterprise (association)" obligates the enterprises to improve the medical care of the workers, to provide an integrated approach to the therapeutic and preventive activity, and to expand and strengthen the therapeutic and preventive system.

All of these factors allow us to expect an increased activity of the enterprises in the financing of the public health by negotiating agreements with the treatment and prevention facilities or by creating and developing their own system of providing medical care to the workers.

In our estimation, a genuinely mixed type of insurance will in fact be developed at the efficiently operating enterprises and in organizations and collective farms that have the ability to devote a certain amount of their resources (for example, from the social insurance fund) to the formation of special insurance funds. By means of these resources, it will be possible to fund the contracts with public health facilities, medical colleges, research institutes, and cooperatives to provide various kinds of therapeutic and sanitary care to the workers and the members of their families, as well as totally finance (including salaries) medical stations or other medical consultative services. If, moreover, the enterprises are allowed to retain a portion of the resources earmarked for the state social insurance and/or a portion of the resources contributed by the enterprises to the state budget in the form of payment for labor resources, the incentive of the work collectives to improve their health will increase substantially.

In order to supervise the volume and quality of therapeutic and preventive care financed by the enterprises, the effectiveness of utilization of the resources, and the compliance of the workers with the recommendations of the doctors with respect to treatment and prevention of illness, it will be advisable to create special subdivisions (commissions, committees, etc.) consisting of physicians (certified doctors), economists, jurists, and other specialists. At present, there are already examples of certain

enterprises whose trade unions monitor the proper use of funds earmarked for the medical cooperatives to provide therapeutic and sanitary services to the workers and check the claims for work performed, the type of services actually provided, and the degree of satisfaction the workers of the enterprise have with them. On the basis of such specialized formations it will be possible to create insurance agencies on the pattern of the hospital savings bank

In the future, it will be possible to convert the organization of the work of the entire official public health service to conditions of full support by the insurance funds that are created. This will create conditions for a competition with the state public health facilities and serve as a stimulus to improve the work efficiency and quality of medical care

Thus, the existing mechanism of financing of public health in our country is holding back the development of the service for protection and strengthening of the health of the population. One of the ways of solving this problem may be the use of elements of medical insurance. This requires careful analysis of the ways, forms, and phases of its introduction. Implementation of the principles of medical insurance in our country is possible through organizations of the hospital savings bank type

#### Footnotes.

1. Gorbachev, M.S., "The socialist ideal and revolutionary restructuring," KOMMUNIST, No 18, 1989, p 18.

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UDC 616-092:612.017.1.064]-022.7:578.828.6]-  
084.4-039.57(470.23-25)

#### The Work of the 'AIDS and ARC' Consultation and Diagnostic Polyclinic

907C0760B Moscow SOVETSKOYE  
ZDRAVOKHRANENIYE in Russian No 6, Jun 90  
pp 45-49

[Article by A. G. Rakhmanova, V. K. Prigozhina, A. Yu. Kolmakov, Yu. K. Chernyshev, S. A. Gordeyev, V. A. Smirnov, G. A. Makarenko, and V. D. Chuprina, Leningrad Institute of Physician's Advanced Training im Kirov, Municipal Infectious Disease Hospital No. 30 im Botkin]

[Text] The AIDS epidemic, which has seized 144 countries and stricken more than 130,000 persons, with around 10 million carriers of the virus, has made it necessary to develop national and global programs to fight this dangerous disease.<sup>11</sup> Given the lack of a vaccine and no effective means of treatment, the most important sector in the strategy of fighting AIDS is the anti-epidemic measures,<sup>4-8</sup> among which those of critical importance are well informed practicing physicians, educational campaigns with the population, and

screening various groups of the population representing the greatest risk of infection (homosexuals, drug users, prostitutes, blood donors, and others), as well as those suffering from ARC infections, for the human immunodeficiency virus (HIV) [1-3, 7].

A well-proportioned system of epidemic inspection to prevent the spread of HIV infections has been organized in our country, one of the constituent parts of which are the anonymous doctor's offices. In Leningrad, an anonymous office was created on the premises of an infectious disease hospital of 1600 beds, with virological, bacteriological, and biochemical laboratories and a pathological anatomy department. The organization of an anonymous office within a major infectious disease hospital was reasonable and also had practical and theoretical justification. The clinical picture of AIDS, its progress, and perhaps, its occurrence, are determined by the ARC infections.<sup>2,4,6,9,10</sup> These are viral, bacterial, protozoan diseases and helminthic invasions well known to the infectious disease specialist, such as pneumocystosis, toxoplasmosis, cryptosporidiosis, herpes simplex, cytomegalovirus infection, infectious mononucleosis, herpes zoster, legionellosis, septic forms of salmonellosis, escherichiosis, listeriosis, and many others. Such patients require observation by an infectious disease specialist capable of deciding on the tactics of the examination, prescribing adequate outpatient treatment, or

finding cause for hospitalization. Furthermore, a suitable laboratory examination for ARC diseases can only be done properly in the setting of an infectious disease hospital. For this very reason, the staff of the anonymous office was made up of infectious disease specialists with special training for AIDS and ARC diseases.

The tasks of the anonymous office—the taking of blood and the issuing of the results of the examination for AIDS—were substantially enlarged during the course of its operation and took on the following directions: therapeutic-diagnostic, organizational-methodological, scientific. As a result, the anonymous office, together with the hospital departments for HIV-infected patients and those suffering from ARC infections and the specialized diagnostic laboratory, became a clinical center for the problem of AIDS not only in the city but also in the region, being named the AIDS Consultation and Diagnostics Office (CDO), and then the Polyclinic Department for AIDS and ARC.

We have analyzed the therapeutic and diagnostic work of the CDO over the year and a half of its activity in 1987-1988. During this period, 15,112 persons underwent laboratory and (when necessary) clinical examination at the CDO, resulting in the discovery of 27 HIV-infected persons. Moreover, the other therapeutic and preventive facilities identified 4 HIV-infected patients, who were subsequently seen by the doctors of the CDO. The composition of the persons examined and the number of HIV infections discovered are shown in Table 1.

**Table 1. The Cohort of Persons Examined at the AIDS CDO and the Number of HIV Infections**

Contingent of examinees	Number examined		Number of HIV infections	
	absolute	%	absolute	%
Examined anonymously	7695	50.92	1	0.013
Examined in accordance with the instructions of the USSR Ministry of Health				
blood donors	62	0.41	1*	—
Soviet citizens returning from trips abroad	963	6.37	—	—
foreign nationals who are students or working here for a lengthy time	579	3.83	19	3.28
persons from risk groups				
blood recipients	51	0.34	—	—
drug addicts	58	0.38	—	—
homo- and bisexuals	33	0.22	3*	—
special UVD group	1520	10.06	—	—
Persons with promiscuous sexual relations	2438	16.13	—	—
Persons coming in contact with HIV-infected patients				
foreign nationals	64	0.43	3	4.69
Soviet citizens (including one child)	48	0.32	2	4.17
Persons examined for clinical indications	1601	10.59	2	0.12
Total	15,112	100	27	0.18

\* Identified during examination at a blood transfusion station.

\*\* Identified as suffering from venereal diseases during examination at dermatology and venereal disease dispensaries.

As is evident from the table, more than half of those examined came anonymously to the CDO, and they were asked voluntarily to fill out a questionnaire and answer a number of questions: age, sex, family status, past diseases (including venereal), whether or not they were a donor or recipient of blood, sperm, organs, had they taken narcotics intravenously, the number of sexual partners during a certain period of time, homosexual contacts, and other questions enabling a medico-sociological investigation of this group of the population. It should be pointed out that only 1894 persons voluntarily filled out the questionnaire in full; the others refused to provide certain information about themselves or did not respond to many questions. Analysis of the anonymous questionnaires revealed that 86.5 percent of those coming to the CDO were 20 - 39 years old, 18.5 percent of those deciding to undergo examination were blood recipients, 12.2 percent had had venereal diseases (gonorrhea, trichomoniasis, syphilis), 9.2 percent had heterosexual contacts with foreign nationals, and 16.6 percent had a sexual partner who had had contact with foreigners. Furthermore, 21.9 percent of the people had more than 5 sexual partners during the last 5 years, and the number of sexual partners was 20 or more for 5.2 percent of those examined.

The group of persons examined for clinical indications, which amounted to 10.59 percent, indirectly characterizes the educational campaign among the population and the alerting of medical workers to HIV infection. It is significant that 75.9 percent of the people of this group came to the CDO of their own accord, on account of worsening health, and only 20.1 percent were sent here by various therapeutic and preventive institutions: 12.8 percent of these by the front-line doctors (polyclinics, medical and sanitary departments, health centers), 1.8 percent by various hospitals in the city, 1.6 percent by the dermatology and venereal disease dispensaries, 0.1 percent by the neurology dispensaries, 3.0 percent by the sanitary epidemiological stations, and 4.0 percent, not by medical institutions but by the UVD [internal affairs administration].

Among those examined for clinical indications, the number of men and women was almost the same (54.1 and 55.9 percent, respectively). Like those examined anonymously, they were primarily persons of young age, 20 - 39 years old (78.4 percent). It was established from their epidemiological case history that 63 percent of them had sexual relations with casual partners and 10.9 percent had homosexual contacts with foreign nationals from countries where HIV infection is endemic. Of those examined, 7.6 percent were being treated for venereal diseases, and 4.5 percent had received blood transfusion or blood products. Most often (81.5 percent of the patients), the reason for coming or being sent to the CDO was periodically recurring temperature rise, usually to the subfebrile level. In addition to fever, 51.7 percent complained of weakness and increasing tiredness. Against the background of subfebrility, 12.7 percent of the patients noticed an increase in the peripheral lymph

nodes, 3.8 percent noticed pain in the joints, 4.0 percent noticed pain in the throat or coughing, and 15.8 percent noticed dysfunction of the intestines, pain in the epigastrium, or unstable stool. A significant loss in body weight was registered in 2.8 percent of those examined; various outbreaks on the skin and mucous membranes were found in 7.5 percent. All these patients required a deeper clinical and laboratory investigation and differential diagnosis to rule out HIV infection in the stage of persisting generalized lymphadenopathy, AIDS-related complex, as well as AIDS-indicating infections. Of these patients, 98.4 percent were examined as outpatients and the others in a specialized department of the hospital. In order to ascertain the diagnosis, various specialists were used to examine the patients. Consultation of a gynecologist was required for 15 percent of the patients, a dermatology and venereal disease specialist for 11 percent, and a phthisiopulmonologist for 3.0 percent. In recent time, persons requiring psychotherapeutic assistance became increasingly more common (3.4 percent), including those suffering from AIDS phobia. Other specialists took part in the examination of the patients: stomatologists, otorhinolaryngologists, neuropathologists.

The examination of the different groups of the city population revealed 31 infected with HIV, among which 19 were foreign nationals and 12 our fellow countrymen. The diagnosis of all of them was verified by the discovery of HIV antibodies in the immuno-enzyme analysis and immunoblotting reactions. The foreign nationals, after the diagnosis was confirmed, were deported from the USSR, and the Soviets were subjected to careful clinical and laboratory examination in a specialized department of the hospital, as a result of which 10 of them were diagnosed with HIV infection in the stage of generalized lymphadenopathy and 2 of them with AIDS-related complex. Of major importance in organizing the examination for AIDS is information on which groups of the population infected with the virus belong to and how to find this out. Of the infected Soviet citizens, one woman was examined anonymously, it was later discovered that she had many sexual partners from African countries; 3 male homosexuals were examined at the CDO as suffering from venereal diseases; 2 women were sent to the CDO for clinical epidemiological indications (1 by a woman's consultation clinic, 1 by a member of the UVD); and 3 women with casual sexual relations were examined on account of contact with infected foreign nationals. One woman, discovered during the blood transfusion stage, was found to be the source of infection of her husband and child.

Prophylactic medical examination holds an important place in the therapeutic and diagnostic activity of the CDO. A total of 270 patients were under dispensary observation: 12 infected with HIV, 64 who came into contact with them, 127 patients with suspicious outcome of the immuno-enzymatic analysis or immunoblotting, 67 suffering from AIDS-indicating infections (herpes, toxoplasmosis, candidiasis), as well as those with generalized lymphadenopathy of undetermined etiology. All

those undergoing dispensary observation were actively submitted for clinical and laboratory investigation, including clinical examination, immunological tests, and serological, bacteriological, and biochemical investigation to rule out AIDS-labeled infections. When necessary, the patients were hospitalized.

Analysis of the therapeutic and diagnostic work of the CDO reveals that its activity over the course of the year has taken on a new organizational form requiring a larger staff of doctors at the expense of various specialists: dermatology and venereal diseases, gynecology, stomatology, psychotherapy, and sexology. It was found necessary to have a records clerk and a statistician on staff. The wisdom of creating a polyclinic department on the premises of a major infectious disease hospital that is capable of providing state-of-the-art laboratory examination of the patients, clinical observation, and treatment by highly trained specialists became obvious. The AIDS and ARC polyclinic department organically grew into an AIDS center.

The creation of a polyclinic department, being a new organizational form of the work of the AIDS service, will promote extensive screening of various groups of the population for HIV infection and identification of infected persons and improve the level of therapeutic and prophylactic care, bringing it as close as possible to the population.

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#### Contemporary Trends in Mortality of "Working" Age Population From Diseases of the Circulatory System

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[Article by Prof. B. A. Voitsekhovich, T. F. Slauta, and V. V. Pilshchikova; Kuban "Red Army" Medical Institute; in HEALTH OF THE POPULATION section]

[Text] A change in the character of pathology in the population has resulted in the fact that, by the end of the century, chronic non-epidemic diseases, especially diseases of the circulatory system, have come to occupy a leading place in the structure of the causes of death in the economically developed countries. They are already the cause of every second death in the USSR and some other countries.

This fact in and of itself should hardly be cause for alarm. Death is an attribute of life, its natural end, and since almost no one dies "under the weight of the years" alone, some cause of death or another must stand behind each instance of death.

As health has improved, the age of death in humans has become more and more advanced; that being the case, of course, cardiovascular diseases (CVD), as the most characteristic for the "autumn" of life, are more and more often the cause of death.

However, CVD are still far from always the cause of death only in the elderly and the aged. They also make up a significant portion in the mortality structure of individuals of working age, thereby reflecting a certain degree of the "growing younger" of cardiovascular pathology. Thus, according to the data of V. A. Bystrova and R. K. Ignateva [2], mortality in the USSR from CVD has increased in all age groups, starting from the age of 30; however, the rate of its increase is highest in the working ages: 34 percent from 30 - 49 years old as opposed to 29 percent in the 65 and older age group.

According to the results of a sample study carried out in Voronezh Oblast [5], 12.3 percent of those dying from hypertensive disease (HD) and ischemic heart disease (IHD) (20.8 percent of men and 5.7 percent of women) were found in the working age group. V. A. Almazov and co-authors [1] have cited data regarding the fact that, among those dying of CVD in Leningrad, individuals in the 20 - 29 year age group constituted 7 percent, in the 30 - 39 year age group 16.4 percent, in the 40 - 49 year age group 30.4 percent, and in the 50 - 59 year age group 42 percent.

The present investigation was carried out for the purpose of a deeper study of the level, time course, and main trends in the mortality of the "working" age population from specific forms of CVD, based on data from the Krasnodar Region in the last 30 years (we are calling the ages from 20 - 59 years the "working" age, as we believe that this term most fully reflects the social essence of this contingent of the population). During this time, there were changes in opinions regarding the diagnosis of CVD and in the classification of class VII diseases. But the diseases we have distinguished (rheumatic fever, HD, IHD, and cerebrovascular lesions) were sufficiently clearly followed through all of these years.

Among all those dying in the Region from CVD, individuals of working age constituted 11.7 percent (21.7 percent of the men and 5.8 percent of the women), while among all those of working age who died, 31 percent were victims of CVD (30.6 percent of the men and 31.4 percent of the women).

The structure of the principal causes of death in the working age population underwent substantial changes during the period under investigation. If CVD occupied second place in men in 1958-59, after trauma, and in women, after neoplastic diseases, in 1985-86 they shared first place with these causes (in both sexes), claiming the life of every third individual.

The level of mortality from CVD in the 30 year period increased significantly in men (by a factor 1.8), while in women it remained practically at the previous level, and a tendency toward decrease was even noted. As a result, the level of total mortality of individuals of working age in 1985-86 turned out to be, overall across the Region, 15.6 percent lower than the corresponding level across the USSR, 20.6 percent lower in men and 10.5 percent lower in women [3]. However, disease of the circulatory system differed in their dynamics (Table 1).

**Table 1. Time Course of the Level of Mortality of the Working Age Population in Krasnodar Region from CVD in 1958-1959, 1969-1970 (1), 1978-1979 (2), 1985-1986 (3) (of the 1958-1959 Level in the Corresponding Gender Groups, Taken as 100)**

Diseases	Men			Women		
	1	2	3	1	2	3
	79.6	67.5	55.5	56.9	49.6	33.8
HD	160.7	75.0	54.8	108.3	55.6	47.2
IHD	189.9	251.0	265.6	93.6	122.0	130.1
Cerebrovascular lesions	138.4	158.6	180.7	122.6	166.3	173.3
Others	136.2	94.9	90.8	52.9	46.5	46.5
On the average	151.6	168.3	176.2	85.7	97.6	96.9

Mortality from rheumatic fever decreased markedly (by a factor of 1.8), and to a much more significant degree (by a factor of 3.0) in women. If in 1958-59 the mortality of working age women from rheumatic fever was higher (by a factor of 1.4) than that in men; 30 years later these figures turned out to be lower in women than in men by a factor of 1.5 - 1.7 across all age groups in the 20 - 49 year interval, while in the 50 - 59 year age group they did not differ substantially.

The most frequent cause of death in the working age from diseases of the circulatory system is IHD. It is not by accident that as far back as 1969 the Executive Committee of WHO warned: "Coronary heart disease has become enormously widespread, afflicting ever younger individuals. In subsequent years this will bring humanity to an enormous epidemic, if we are not up to the task of changing this trend on the basis of research concentrated on the study of the cause and prevention of the disease". In the period under investigation, mortality from IHD increased by a factor of 2.7 in men, especially in the 40 - 59 year age group, and at the present time occupies the principal place in the structure of mortality from CVD (59.4 percent) leaving all other diseases of

this class far behind, since the rate of increase in mortality from IHD has exceeded the movement of mortality from all other diseases of the circulatory system, taken together, by a factor of 1.5. Mortality from IHD increased in women to a significantly lesser degree (by 23.2 percent), and comprises 37.4 percent in the structure of mortality from CVD, yielding only to cerebrovascular lesions. The difference in mortality from IHD in men and women is also highly significant. If at the beginning of the period, the level of these figures in the former was higher by a factor of 1.9, at the end it was higher by a factor of 3.9, and in all age groups the mortality rates in working age men was higher than in women. However, since IHD is a collective concept, which includes an entire group of diseases (myocardial infarction, post-infarct cardiosclerosis, angina pectoris, and other forms), the approach to diagnosis, and accordingly to the coding of the diagnosis for analysis of the primary statistical material is made more difficult, inasmuch as it is often difficult to single out one form of IHD as the principal cause of death, all the more so since each of them includes a set of diagnoses.

The mortality rates from cerebrovascular lesions increased over the 30 years to an equal degree in men (by

a factor of 1.8) and in women (by a factor of 1.7). However, if in working age men every fourth case of death from CVD

is associated with cerebrovascular lesions, in women it is every second to third case (Table 2).

**Table 2. Time Course of the Level of Mortality of the Working Age Population in Krasnodar Region from CVD in 1958-1959 (1), 1969-1970 (2), 1978-1979 (3), 1985-1986 (4) (of the Total in the Corresponding Gender Groups)**

Diseases	Men				Women			
	1	2	3	4	1	2	3	4
Rheumatic fever	13.9	7.3	5.6	4.4	25.6	17.0	13.1	8.9
HD	6.1	6.5	2.7	1.9	7.1	9.0	4.0	3.5
IHD	39.5	49.4	58.9	59.4	27.8	30.4	34.7	37.4
Cerebrovascular lesions	26.3	24.0	24.8	27.0	24.0	34.3	40.8	42.8
Others	14.2	12.8	8.0	7.3	15.5	9.3	7.4	7.4

By comparing the levels of mortality of working age individuals from HD at the beginning and end of the period in question, we found them to be markedly decreased: by a factor of 1.8 in men and by a factor of 2.1 in women. A similar trend has been followed in many economically developed countries (Table 3).

**Table 3. Time Course of the Mortality Rates of the Working Age Population from HD (per 100,000 Individuals of the Corresponding Gender)\***

Country	Year	Gender	
		m.	f.
Japan	1960	10.1	8.5
	1982	0.9	0.7
USA	1960	12.1	7.8
	1982	2.1	1.2
Canada	1960	25.6	22.5
	1982	8.2	5.2
	1960	11.1	10.1
	1982	2.1	1.4

However, a significant decrease in mortality from HD in no way indicates a decrease in the prevalence of this disease. This is explained by the fact that, in indicating HD as a principal cause of death, the physician has in mind one of the outcomes or complications of this disease, other than IHD and cerebrovascular lesions, which are the most frequent complications of HD, but which are coded with other rubrics of the International Statistical Classification of Diseases, Traumas, and Causes of Death. In addition, in the current practice of analysis of mortality data, a situation frequently arises in which in the case of a combination of IHD or cerebrovascular lesion with HD and the necessity of choosing one cause of death, preference is given to the first disease, and HD is practically ignored. Therefore, the rate of death from HD without account being taken of mortality from its principal complications is, in essence, the only one among all other mortality rates

from CVD which does not give a complete representation of the true prevalence of this disease.

Moreover, the level of mortality rates from all causes, including diseases of the circulatory system, in many ways depends on the method of selection of the principal cause of death. As B. Ts. Uralanis asserted [4], "each step in the refinement of the determination of the causes of death would to some extent promote an increase in the lifespan". But, in striving for superfluous specification of the causes of death in which the choosing of one disease of the principal causes is required (and it is precisely this principle which underlies traditional mortality statistics), there is a real danger of losing the true representation of the frequency of many diseases and of their significance, since one disease does not always reflect to the necessary degree those pathological processes which have induced death [2]. Only a shift to the study of multiple causes of death will permit the correct assessment of the role of each of the diseases in the occurrence of death.

Thus, in analyzing the mortality of working age individuals from diseases of the circulatory system throughout the Krasnodar Region during the 1958-86 period, its stable growth in men and its relative stabilization in women can be noted. The tendencies identified have made it possible to achieve the prediction of the level of mortality of this contingent of the population in 1999-2000 by the method of extrapolation. The data obtained indicate that by the year 2000 the mortality rate in men from CVD will increase, as compared with 1985-86, by 19.4 percent, while in comparison with 1958-59, it will increase by a factor of 2.1; in women it will remain practically at the previous level and will be 95.8 percent of the 1985-86 level and 98.8 percent of the 1958-59 level.

It is generally recognized that the existing socioeconomic conditions of the life of society which determine the state of its health are refracted through the mortality of the population as through a prism. Having already commenced in the working age, diseases of the circulatory system determine the mortality level in many ways, not

only in this age group but in the older age groups as well. The steady increase in mortality, especially of men, in working age insistently demands urgent solution of organizational problems in the prevention and treatment of diseases of the circulatory system, which in the final result will serve the enhancement of the health of the population.

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#### Study of the Epidemiological Aspects of Tobacco Smoking in Connection With its Clinical Course Among 20-69 Year Old Men of Kiev

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[Article by L. V. Shuteeva and S. P. Garnitskiy; N. D. Strazhesko Kiev Scientific Research Institute of Cardiology (Dir. Prof. N. K. Furkalo)]

[Text] At the present time the campaign against smoking has taken on tremendous socioeconomic significance in connection with the fact that smoking is one of the most important characteristics determining human health, and a factor promoting the occurrence and progression of cardiovascular, and a number of other widespread, chronic noninfectious diseases [1, 3, 7, 8, 10].

Research carried out in the last 10-20 years in the USSR and other countries of the world has demonstrated that stopping the growth, decreasing the prevalence, and reducing mortality from cardiovascular and other chronic noninfectious diseases can only be accomplished by means of scientifically substantiated prophylactic measures [2, 4, 6, 9, 11-13].

Until recently the results of the majority of the investigations that have been carried out have attested to the insignificant effectiveness of behavioral programs to combat smoking among the adult population. A very high frequency of recidivists has been observed in these investigations, and the recidivist curve has been similar

to the corresponding curves obtained in investigations of the effectiveness of programs for the treatment of alcoholism and substance abuse [14]. Therefore, in order to successfully carry out measures against smoking at the populational level, it is necessary to take into account the formation of drug dependency, requiring treatment interventions, on tobacco smoke.

The purpose of this investigation was to study the prevalence and intensity of smoking in connection with the clinical course of tobacco smoking among the unorganized male population, aged 20-69 years, of one of the districts of Kiev. This investigation was carried out within the framework of the "Epidemiological Study of the Prevalence of IHD Risk Factors in Men Aged 20-69 Years Based on the Example of One of the Districts of Kiev" by order of the State Committee of the Council of Ministers of the USSR on Science and Technology [GKNT].

The material of the investigation was a random sample of the non-organized male population in the 20-69 year age groups of one of the districts of Kiev. The random sample was formed on the basis of voters' lists by means of random number tables. In all, 1500 individuals were examined (the response rate was 76.1 percent).

The smoking habit was studied using the standard WHO questionnaire (Rose, Blackburn, 1968), which includes information on the method of smoking, its duration, and the age of onset of smoking. Individuals who smoke at least one cigarette [sigaret] or cardboard-tipped cigarette [papiro] per day for not less than one year up to the time of examination, or who had stopped regular smoking less than one year up to the time of investigation, were considered regular smokers. Individuals who had regularly smoked and who had given up smoking more than one year prior to the time of the investigation were assigned to the group of past smokers. Individuals who had never smoked previously, or who smoked irregularly at the present time, and did not have the habit of daily smoking, were classified as never having smoked. All smokers were divided into subgroups on the basis of the intensity of smoking: those who smoke up to 10 cigarettes a day and those smoking 10-20 or more cigarettes a day.

The statistical analysis of the material was performed on an ES-1035 computer using BMIDP-77 and SAS program packages.

It can be seen from Table 1 and Figure 1 that the prevalence of smoking in the population changed with age. It was greatest in the 20-29 year group at 60.5 percent; of these 31.5 percent smoked up to 10 cigarettes per day, 57.8 percent from 10-20 per day; 10.7 percent were inveterate smokers, who smoke more than 20 cigarettes per day. The fact that 11 percent of the men had already given up smoking by this age, and only 28.5 percent had never smoked was impressive.

Prevalence of Smoking Among 20-69 Year Old Men ( $X^2 = 86.77; p = 0.0001$ )

Age, years	Prevalence of smoking, %					
	nonsmokers	p	past smokers	p	all present smokers	p
20-29	28.5		11.0		60.5	
		>0.1		>0.05		<0.05
30-39	30.5		18.6		50.9	
		>0.05		<0.05		>0.1
40-49	26.0		24.3		49.7	
		<0.02		<0.01		<0.01
50-59	20.5		41.1		38.4	
		>0.1		>0.05		<0.05
60-69	21.6		45.6		32.8	
Age-standardized rate	27		21.9		31.1	

The frequency of smoking decreased with age. By age 30, 50.9 percent are smokers. In this age decade a sharp increase is observed in the group of inveterate smokers (32.9 percent), and the smallest group of infrequent smokers (13.2 percent).

In the 40 - 49 age group, the frequency of smoking decreased insignificantly and made up 49.7 percent; the number of inveterate smokers decreased insignificantly (these constituted 23 percent); at the same time the group of past smokers continued to increase (24.3 percent). In the group of individuals aged 50 - 59, 38.4 percent smoked. The number of individuals who had smoked in the past, increased by a factor of 2, compared with the previous decade and increased by a factor of 4, as compared with the group of individuals aged 20 - 29 years, was observed in this age decade. The prevalence of smoking in the group of individuals aged 60 - 69 years was now 32.8 percent, and was the lowest. The number of individuals who had never smoked fluctuated insignificantly in all age groups, from 20 - 30 percent.

When we studied the structure of smoking, we discovered that the time course of its prevalence and intensity

with respect to age corresponds to the time course of the formation and course of drug dependency on tobacco smoke.

Tobacco smoking, which is one of the forms of common addictions, has a characteristic time course, a definite stereotype of development, and the characteristic clinical features of the syndrome of addiction to a narcotic. The principal among these are the features of dependency (craving, abstinence syndrome) and the features of altered reactivity (change in tolerance) [5].

The structure of the intensity of smoking in the 20's presented in the figure corresponds to the first (initial) stage of tobacco smoking, which is characterized by low intensity. Craving for smoking is determined by psychological dependency and is subjectively pleasant; physical dependency is absent. This is manifested in the fact that the group of inveterate smokers is smallest at this age (10.7 percent), while the group of infrequent smokers is the largest (31.5 percent), i. e., tolerance to tobacco smoke is low.

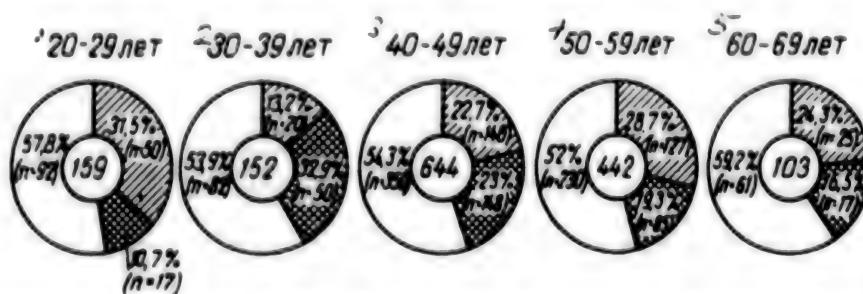


Fig. 1. The prevalence of smokers as a function of the intensity of smoking. The portion of the circle with oblique hatching, those smoking up to 10 cigarettes per day; without hatching, those smoking 10 to 20 cigarettes per day; with cross-hatching, those smoking more than 20 cigarettes per day. In the center of the circle, the total number of subjects by age decades.

Key: 1. 20-29 years—2. 30-39 years—3 . 40-49 years—4. 50-59 years—5. 60-69 years

The structure of the intensity of smoking in the 30 - 39 year age group corresponds to the second stage (the stage of stabilization), which is characterized, along with psychological dependency, by the appearance of physical dependency as well, and by the formation of the abstinence syndrome. At the same time, the most important feature is the increase in tolerance to tobacco smoke and its reaching its maximum. A three-fold increase in the group of inveterate smokers, reaching its maximal size (32.9 percent), takes place at this age. The group of mid-intensity smokers decreases, and the group of infrequent smokers decreases almost three-fold, which confirms the growth and establishment of maximal tolerance to tobacco smoke in this age group.

In the 40 - 49 year age group a correspondence is observed of the structure of the intensity of smoking to the third stage (the stage of pronounced abstinence), the principal features of which are an increase in physical dependency and in the manifestations of abstinence, and the stabilization and beginning of a decrease in tolerance to tobacco smoke. This is reflected in an increase in the size of the group of inveterate smokers, and the stabilization of the size of the mid-intensity smoking group; in addition, an increase begins in the number of infrequent smokers.

The groups of 50 - 59 and 60 - 69 year old individuals correspond in the intensity of smoking to the fourth (terminal) stage of tobacco smoking, which forms after 25 - 30 years of continuous smoking, and is characterized by markedly pronounced physical dependency, complete absence of psychological dependency, severe manifestations of abstinence, and by a decrease in tolerance to tobacco smoke. This is expressed in a constant decrease in the size of the groups of inveterate smokers and an increase in the size of the group of infrequent smokers.

Thus, the data presented indicate widespread smoking among the population, and consequently attest to the necessity of searching for ways and means to combat smoking. At the same time, the prevalence of smoking and its intensity in the age range reflect the stages of the clinical course of tobacco smoking and drug dependency on tobacco smoke. Because of this the data on the prevalence of smoking which take its structure into account permit the development of a differentiated approach to the conduct of measures against smoking among the population, and the resolving of the question as to whether health information, education, and upbringing measures directed toward the formation of a healthy lifestyle have been carried out sufficiently, or whether it is necessary to supplement them with treatment measures.

#### CONCLUSIONS

1. The prevalence of smoking is 51.1 percent in the population of men examined, aged 20 - 69 years. One out

of ten smoke more than 20 cigarettes a day, and one out of four men smoke from 10 to 20.

2. The number of smokers decreases sequentially with age, from 61 percent at age 20 - 29 years to 33 percent at age 60 - 69 years.
3. A correspondence was established between the intensity of smoking by age groups and the time course of the formation and course of drug dependency on tobacco smoke.
4. In the planning of measures in the campaign against smoking, data on the prevalence of smoking, which takes into account its structure, is necessary for the determination of the extent of treatment measures to be taken in the population.

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**Special Selection of Personnel Working With Nuclear Weapons**

907C0710B Moscow ARGUMENTY I FAKTY  
in Russian No 18, 5-11 May 90 p 8

[Article by O. Izvekova]

[Text] "Who serves combat duty with nuclear missiles? Do these people undergo any kind of special selection?"  
Ye. Nikitin, Ust-Kamenogorsk.

According to the USSR Ministry of Defense all work with nuclear weapons is done only by officers and warrant officers that have undergone special training.

A unit commission (of experts) certifies every officer and warrant officer for independent work each year with the participation of a military medical commission. The moral and working qualities and the mental and physical state of the servicemen are checked out in this case. Each year around 4 - 6 percent of officers and warrant officers serving in units operating nuclear weapons are barred from such work on the basis of the results of this selection. This information is not secret, but it has never been made public.

During the tests, military psychologists employ special procedures and create certain psychological stresses for people participating in selection. As a result of this, a number of candidates who fail the tests are not permitted to work with nuclear weapons.

UDC 615.281:578.833.26]036.076.9

### Comparative Assessment of Antiviral Efficacy of Virazole and Ribamydil Against Experimental Lassa Fever in Monkeys

907C07564 Moscow VOPROSY VIRUSOLOGII  
in Russian Vol 35 No 2, Mar-Apr 90 pp 151-152

[Article by V. I. Dvoretskaya, A. A. Yevseyev, G. V. Bogatikov, and V. A. Pshenichnov, Scientific Research Institute of Microbiology, USSR Ministry of Defense, Zagorsk]

[Text] The antiviral action of virazole and its analogues in relation to Lassa virus and some other arenaviruses was demonstrated in experiments both *in vitro*<sup>3-5</sup> and *in vivo*.<sup>7-11,16-18</sup> This preparation also underwent clinical tests in relation to Lassa fever in people,<sup>12-15</sup> and it was recommended as an effective antiviral agent against this disease.

In connection with the acquisition of a Soviet analogue of virazole—ribamydil—and successful study of its action in relation to some infections by the Organic Synthesis Institute of the Latvian SSR Academy of Sciences, it was suitable to assess its efficacy in relation to Lassa fever agent in experiments on primates.

This paper presents the results of a comparative assessment of the antiviral efficacy of the above-indicated chemical preparations in relation to experimental Lassa fever in aerogenically infected monkeys.

#### Materials and Methods

**Virus.** Lassa virus (Sierra Leone strain) maintained by passages in green marmosets (*Cercopithecus aethiops*) were used. The virus culture was a 20 percent suspension of homogenized liver tissue from a monkey infected with Lassa virus.

**Animals.** Research was conducted on hamadryas baboons (*Papio hamadryas*) weighing 4 - 6 kg.

**Chemical Preparations.** The efficacy of ribamydil, formulated for injection and synthesized in the Organic Synthesis Institute of the Latvian SSR Academy of Sciences, was assessed in comparison with the imported commercial chemical preparation virazole, produced by Farmacos Prizzen on the basis of a license from JCN Pharmaceuticals (USA), formulated in capsules for oral administration.

The animals were infected aerogenically at a dose of 15 - 20 PFU per monkey. The chemical preparations were injected intramuscularly into the animals in accordance with two schemes—emergency preventive and therapeutic. In the former cases the preparations were administered two hours after infection and subsequently twice a day for 10 days at a dose rate equivalent to that used in treating Lassa fever in people (600 - 800 mg per day for 10 days). The shock dose for monkeys was 20 mg/kg, followed subsequently by 10 mg/kg twice a day for 10 days. In the latter case the preparations were administered at a similar dose rate when symptoms of disease (fever) appeared in infected animals.

The virus concentration was determined by the commonly accepted procedure of negative colonies, by titration in a CMK cell culture (inoculated line of kidney cells from the green marmoset).

#### Results and Discussion

Preliminary study of the peculiarities in the course of illness in monkeys experimentally infected with Lassa virus showed that it recalls published descriptions of Lassa fever in man. These observations are consistent with data of foreign researchers.<sup>6,10</sup> The antiviral efficacy of the chemical preparations was assessed on the basis of the percent of protection and average life span and level of viremia. Average life span was calculated in each group on the basis of all animals, conditionally assuming that it corresponds to the period of observation of the animals in the experiment.

The results of comparatively assessing the therapeutic efficacy of ribamydil and virazole against experimental Lassa fever in aerogenically infected animals are shown in the table.

Therapeutic Efficacy of Ribamydil and Virazole Against Experimental Lassa Fever in Aerogenically Infected Monkeys

Preparation	Preparation Administration Scheme	Number of Infected Animals	Efficacy Indicator			
			Number of Animals Surviving	Average Life Span, Days	Average Time of Death, Days	Virus Concentration in Blood Serum, Ig PFU/ml
Ribamydil	Emergency preventive	5	3	25 +/- 3	19 +/- 2	2.2 +/- 0.4
	Therapeutic	5	3	25 +/- 3	19 +/- 2	2.5 +/- 0.1
Virazole (control)	Therapeutic	4	2	25 +/- 3	20 +/- 2	2.4 +/- 0.1
Without preparation (control)	-	4	0	15 +/- 1	15 +/- 1	4.5 +/- 0.2

These data show that Lassa virus administered to monkeys by the aerogenic pathway elicits lethal illness in them, modeling the serious course of Lassa fever in people. The Soviet analogue of virazole—ribamydil—is not inferior in antiviral efficacy to the imported preparation, and it significantly increases the number of surviving animals in comparison with the group not subjected to therapy. The number of surviving animals in the case of emergency prevention and treatment with ribamydil was 60 percent, which is not any lower than the same indicator obtained when using virazole, in which case 50 percent of monkeys infected with Lassa virus survived. The average life span of animals also increased significantly when ribamydil was used, and it was similar to that of animals subjected to virazole therapy.

As a result of treatment with ribamydil as well as with virazole, the concentration of virus in blood serum decreased significantly (by a factor of almost 100) in comparison with the same indicator for the group of animals that did not receive the preparation.

Our results are consistent with the data of foreign researchers who studied the efficacy of virazole against parenteral infection of monkeys with Lassa virus.<sup>9</sup>

11.17.18

Manifestations of toxic action of the preparations were not noted in our research in the group of uninfected hamadryas baboons to which virazole or ribamydil was administered (similarly as with infected baboons). All of the indicated animals remained alive. However, virazole and ribamydil obviously did have a side effect on the monkeys. Judging from the data of foreign authors<sup>19</sup> who evaluated the change in blood indicators in response to a course of virazole treatment in similar experiments on monkeys, a decrease in the number of erythrocytes and, to a lesser degree, reticulocytes, growth of the number of thrombocytes, and a reduction of the concentration of hemoglobin and the hematocrit are observed. Changes in white blood cell indicators were insignificant. However, according to the data of the authors cited above, all of the noted deviations returned to their initial level 3 - 4 weeks after administration of the preparation was terminated.

There is special interest in studying the action of virazole and ribamydil on the immune status of the body and on the functional activity of immunocompetent cells. The immunodepressive action of virazole noted by a number of authors obviously does not hinder recovery from Lassa fever. When certain immunodepressants (azathioprine, methotrexate) were administered, a protective effect was observed in 40 - 50 percent of mice infected with Lassa virus.<sup>2</sup> The role of immunity modulating properties of anomalous nucleosides in the presence of Lassa virus is a problem requiring special research.

Thus it is demonstrated that when administered parenterally, the Soviet analog of virazole—ribamydil formulated for injection—is effective against experimental

infection in monkeys that is elicited by aerogenic administration of Lassa virus. It is also demonstrated that it does not differ significantly from virazole in its degree of action.

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#### **Antisense RNA for Treatment of Viral Encephalitis**

907C0756B Moscow ZNANIYE-SILA in Russian No 6, Jun 90 p 25

[Article: "On the Usefulness of Disinformation", unattributed]

[Text] Since some time ago, geneticists have been using the concept of "antisense" in application to genetic information. To be more accurate, this is sooner "dis-" than "anti-information." It is contrary, supplementary or (in scientific language), complementary to the principal information encoded in the nucleotide sequence of long RNA and DNA molecules. And its usefulness has been revealed in some experiments. It turns out that short RNA segments suppress duplication of viruses, but only if the "antisense" of the structure of the RNA of the viruses themselves is contained within these segments. Then prospects open up for a new means of fighting viral infection: We must clarify the nucleotide sequence in the viral RNA, make antisense copies of some of its segments, and use them against the virus. In some, as yet incomprehensible way, segments of this false genetic information are built into the virus's duplication mechanism, everything there becomes confused, and as a result duplication ceases, which is equivalent to victory over infection. This possibility had to be verified experimentally.

Tick-borne encephalitis virus was selected for experiments conducted in Moscow's Institute of Poliomyelitis and Viral Encephalitis of the USSR Academy of Medical Sciences and in Novosibirsk's Bio-Organic Chemistry Institute of the Siberian Department of the USSR Academy of Sciences. Scientists synthesized RNA segments corresponding to different sections of the virus in which the nucleotide sequence was repeated precisely "back to front." Then mice were infected with real virus, and the scientists began introducing solutions containing false copies into them.

Animals in the control group, which were infected but which did not receive injections of viral disinformation, died of encephalitis by the tenth day. Half of the ones receiving the injections also died. But the most important thing lies in something else. The surviving animals acquired stable immunity to this infection: With repeat infection by the virus, they did not fall ill at all!

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UDC 616.98:578.6]-07:616.157-078.73

#### **Standard Panel of HIV Positive and Negative Human Sera for Assessment of Sensitivity and Specificity of Diagnostic Immunoenzyme Kits**

907C0757A Moscow VOPROSY VIRUSOLOGII  
in Russian Vol 35 No 2, Mar-Apr 90 pp 125-128

[Article by M. S. Vorobyeva, T. D. Shalamberidze, G. V. Fedorova, Z. K. Suvorova, V. V. Pokrovskiy, M. O. Daulina, A. L. Liozner and Ye. M. Yefremova, State Institute of Standardization and Control imeni L. A. Tarasevich and Central Scientific Research Institute of Epidemiology, USSR Ministry of Health, Moscow]

[Abstract] Five Soviet and foreign diagnostic immunoenzyme kits were tested against a panel of 40 HIV antibody negative and 50 HIV antibody positive sera. None of the negative sera gave a false-positive result. However, most positive sera gave positive results at higher dilutions than those recommended in the instructions for indirect immunoenzyme kits, with one serum giving a false negative result. A higher incidence of false negative results was obtained with direct kits. Finally, all HIV positive sera gave positive results in immunoblotting studies. Accordingly, the panel was adopted at nine Soviet research establishments for monitoring the sensitivity and specificity of diagnostic kits for HIV antibody. Tables 1; references 18: 1 Russian, 17 Western.

UDC 616.98-022-078.73

#### **Stability of Major Components of Enzyme Immunoassay for AIDS Diagnosis**

907C0757B Moscow VOPROSY VIRUSOLOGII  
in Russian Vol 35 No 2, Mar-Apr 90 pp 128-130

[Article by S. S. Marenikova, E. M. Shelukhina, E. V. Chekunova, G. R. Matsevich and S. D. Zayko, Scientific Research Institute of Viral Preparations, USSR Academy of Medical Sciences, Moscow]

[Abstract] An analysis was conducted on the stability of two major reagents of enzyme immunoassay systems: HIV-sensitized polystyrene adsorbent and peroxidase-antibody conjugate. The results demonstrated that stability, sensitivity and reliability of the assays kits were enhanced by ensuring an adequate concentration of HIV antigen on the adsorbent. In addition, stability of the peroxidase conjugate was found to be predicated on the lyophilization process and readily assessed from the level of activity remaining after heat treatment at 100°C for 1 h. Judicious adjustment of the components for proper concentration and thermal stability was found to be an effective means of extending the shelf-life of these kits to 6 months from the present 3 month expiration limits. Figures 1; tables 4.

UDC 615.371:578.821.5].015.4.076.9

**Stimulation of Spontaneous and Induced Neoplasms in Mice by Vaccinia Virus**907C0757C Moscow VOPROSY VIRUSOLOGII  
in Russian Vol 35 No 2, Mar-Apr 90 pp 130-132

[Article by N. A. Kharkovskaya, Z. I. Merekalova and S. A. Khrustalev, Laboratory of Viral Carcinogenesis, Department of Laboratory Animals, All-Union Oncologic Scientific Center, USSR Academy of Medical Sciences, Moscow]

[Abstract] A series of experiments were conducted on male and female BALB/cJLacSto mice to assess the effects of vaccinia virus vaccine on spontaneous and Rauscher virus-induced neoplasms. The results demonstrated that scarification of two month old mice with the vaccinia virus led to a statistically significant elevation in the incidence of spontaneous benign and malignant neoplasms, both solid tumors and leukemias. Vaccination before or after intraperitoneal administration of Rauscher virus in a dose of 0.01 or 0.001 ID<sub>50</sub>/ml resulted in leukemia in 48 and 11.5 percent of the animals, respectively, whereas mice not exposed to the vaccinia virus remained free of the malignancy. The tumor-promoting activity of vaccinia virus was attributed, at least in part, to its immunosuppressive properties and stimulation of cell division. Figures 1; tables 2; references 13: 8 Russian, 5 Western.

UDC 615.371:[578.821.5+579.891].036.8

**Clinical Trials With Recombinant Smallpox-Hepatitis B Vaccine in Volunteers**907C0757D Moscow VOPROSY VIRUSOLOGII  
in Russian Vol 35 No 2, Mar-Apr 90 pp 132-135

[Article by V. I. Chernos, N. V. Chelyapov, T. P. Antonova, L. Ye. Rakhilina, S. S. Unanov, A. D. Altshteyn, L. G. Zakharova, I. I. Fodor, K. A. Bendukidze, F. I. Komarov, B. P. Belyshev, A. V. Dmitriev and O. G. Andzhaparidze, Scientific Research Institute of Viral Preparations, USSR Academy of Medical Sciences, Moscow; Institutes of General Genetics, Moscow, and of Biochemistry and Physiology of Microorganisms, Pushchino-on-Oka, USSR Academy of Sciences]

[Abstract] Clinical trials were conducted on 20 male volunteers, 18 - 20 years old, to assess the safety, reactogenicity, and efficacy of a live recombinant smallpox-hepatitis B (RSHB) vaccine. RSHB vaccine was constructed by inserting the S gene of hepatitis B virus into the LIVP vaccine strain of the smallpox virus. Immunological, clinical and biochemical monitoring of the subjects showed good tolerance of RSHB with essentially minimal reactogenicity, and antibody production against the smallpox virus, but not against HBsAg. Revaccination with RSHB after 45 days elicited an anamnestic response against the smallpox virus, but not

against HBsAg. However, such individuals were primed to respond with much higher antibody titers against HBsAg following vaccination with inactivated plasma hepatitis B vaccine. Figures 1; tables 2; references 8: 2 Russian, 6 Western.

UDC 616.36-002.7:578.891]-085.373:578.245]-036.8

**Effects of Recombinant IFN-A<sub>2</sub> on Interferon Status of Hepatitis B Patients**907C0757E Moscow VOPROSY VIRUSOLOGII  
in Russian Vol 35 No 2, Mar-Apr 90 pp 135-138

[Article by V. I. Pokrovskiy, V. V. Malinovskaya, R. T. Murzabayev, V. I. Vasilyeva and A. A. Asratyan, Central Scientific Research Institute of Epidemiology, USSR Ministry of Health; Institute of Epidemiology and Microbiology imeni N. F. Gamaleya, USSR Academy of Medical Sciences, Moscow]

[Abstract] Clinical trials were conducted on 152 patients, 16 - 65 years old, with acute hepatitis B (AHB) to assess the benefits of recombinant IFN-A<sub>2</sub>. Control data on interferon (IFN) status clinical course were derived from AHB patients treated conventionally without IFN-A<sub>2</sub>, as well from healthy controls. IFN-A<sub>2</sub> was administered i.v. and i.m. in doses of 10<sup>6</sup> IU b.i.d. for five to ten days. Control data from the healthy cohort showed virtual absence of plasma IFN, while induction studies with leukocytes yielded ca. 403 IU/ml of IFN, and with lymphocytes ca. 137 IU of IFN- $\gamma$ /ml. Patients with AHB, prior to treatment, displayed elevated serum levels of IFN (6.7 IU/ml), combined with depression of leukocytic production of IFN- $\alpha$  and - $\gamma$  to 9 - 9.7 percent of control level. Treatment with recombinant IFN-A<sub>2</sub> had a beneficial effect on the clinical course and IFN production, accelerating more complete recovery and precluding progression to chronic hepatitis. Best results were seen in AHB patients treated early in the disease with IFN-A<sub>2</sub>, who also presented with a marked improvement in their IFN status. The study also demonstrated that monitoring the IFN status of patients with AHB provides meaningful prognostic criteria. Figures 3; references 13: 8 Russian, 5 Western.

UDC 615.281:578.245.2].076.9

**Antiviral Efficacy of Amixin and its Effects on Interferon (IFN) Status in Mouse Hepatitis**907C0757F Moscow VOPROSY VIRUSOLOGII  
in Russian Vol 35 No 2, Mar-Apr 90 pp 138-140

[Article by S. S. Grigoryan, A. M. Ivanova and F. I. Yershov, Institute of Epidemiology and Microbiology imeni N. F. Gamaleya, USSR Academy of Medical Sciences, Moscow]

[Abstract] Mouse trials were conducted on Amixin [sic], a low MW Soviet IFN inducer, vis-a-vis infection with mouse hepatitis virus and IFN status. Amixin—

2,7-bis[2-(diethylaminoethoxy)-9OH dihydrochloride—was administered per os in a dose of 4 mg/mouse to 16 - 18 g mice one to seven days before the animals were infected per os with 0.2 - 0.3 ml of a 30 - 40 percent suspension of the mouse hepatitis virus. Amixin was found to induce a rapid rise in serum IFN, reaching a maximum of 1280 U/ml in 24 h (20 - 80 U/ml in 48 - 72 h), with reduction of the mortality rate to 40 - 50 percent if infection followed in 24 - 72 h, versus a control mortality rate of 100 percent. However, infection after 72 h reduced the survival rate to 10 - 20 percent, and after 7 days the mortality rate was 100 percent. Concomitant evaluation of the IFN status showed that amixin led to a 8- to 10-fold increase in IFN- $\alpha$  and - $\gamma$  production by splenic lymphocytes control levels. In amixin-untreated mice infection resulted in depression of IFN- $\alpha$  and - $\gamma$  synthesis. These observations demonstrated that prophylactic administration of amixin was effective in reducing mortality due to mouse hepatitis virus and in improving the IFN status of animals. Accordingly, the data indicate that amixin should be considered for prevention of human hepatitis A. Figures 2; tables 2; references 7: 4 Russian, 3 Western.

UDC 578.833.26:578.23].08

#### Lysosomotropic Agents Inhibiting Arenavirus Infection of BHK-21 and Vero Cells

907C0757G Moscow VOPROSY VIRUSOLOGII  
in Russian Vol 35 No 2, Mar-Apr 90 pp 146-150

[Article by S. Ye. Glushakova, A. I. Yakuba, A. D. Vasyuchkov, R. F. Maryankova, T. M. Kukareko, T. A. Stelmakh, T. P. Kurash and I. S. Lukashevich, Belorussian Scientific Research Institute of Epidemiology and Microbiology, Belorussian SSR Ministry of Health, Minsk]

[Abstract] A series of agents acting on lysosomes were evaluated for their effects on adsorption and ingress of arenaviruses into cells, in order to determine whether a pH-dependent mechanism was involved in the initiation of infection. The study relied on BHK-21 and Vero continuous cell cultures pretreated with ammonium chloride, monensin, amantadine, or chloroquine for 1 h prior to exposure to Lassa, Mozambique or Pichinde AN 3839 arenaviruses. The results showed that pretreatment of the cells with agents that effect an increase in the pH of cell organelles from ca. 4.8 to 5.0 - 6.0 leads to virtually complete inhibition of arenavirus replication. The study also revealed that the Mozambique virus was 20- to 40-times as susceptible to the effects of these agents as the Pichinde and Lassa viruses, an interesting difference in view of the serologic relatedness of the Lassa and Mozambique viruses. In addition, complete inhibition of Mozambique virus replication was obtained even on simultaneous addition of the virus and ammonium chloride to the cultures. Finally, the earliest stages of virus-cell interaction, i.e., adhesion, were

observed to be most susceptible to the action of the agents in question. Figures 6; tables 1; references 16: 2 Russian, 14 Western.

UDC 578.828.6:[578.1]:577.152.344

#### Properties of Human Immunodeficiency Virus Protease Synthesized in Escherichia Coli Bacteria

907C0856B Moscow VOPROSY VIRUSOLOGII  
in Russian Vol 35 No 3, May-Jun 90 pp 206-208

[Article by S. V. Shulnenin, N. I. Tarasova, S. V. Gulnik, A. F. Bobkov, A. A. Bogdanov, V. M. Stepanov, and M. M. Garayev, Virology Institute imeni D. I. Ivanovskiy, USSR Academy of Medical Sciences; Moscow State University imeni M. V. Lomonosov, Moscow]

[Abstract] The expression and enzymatic activity of the human immunodeficiency virus-specific protease, whose activity is essential to the formation of infectious virus particles, in *Escherichia coli* cells was studied and a simple system for testing this protease's activity was designed. Immunoblotting was employed to determine the presence of specific protease activity in lysates of HB101/pPR6 bacteria. Electrophoretic analysis of p165 preparations treated with bacteria extracts containing the pPR6 hybrid plasmid demonstrated a decrease in the intensity of the 165 kD fraction and the appearance of bands with molecular masses of 42, 28, 23, and 19 kD, all of which contain antigenic HIV determinants. These findings demonstrate that the active virus-specific protease is synthesized in *E. coli*. Furthermore, results indicate that this technique for determining HIV protease activity may be employed for screening chemopreparations as possible specific inhibitors of this enzyme. Figures 3; references 13: 3 Russian, 10 Western.

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#### Interferon-Inducing Activity of Lassa Virus in Inbred Mice

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[Article by B. I. Zudin, A. N. Rozdyalovskiy, and A. S. Petkevich, Belorussian Epidemiology and Microbiology Scientific Research Institute, Belorussian Soviet Socialist Republic Ministry of Health, Minsk; Institute of Nuclear Energy, BSSR Academy of Sciences, Minsk]

[Abstract] The ability of the Lassa virus to induce the production of interferon, which has been shown to significantly alter arenavirus infection, was studied in the experimental infection of inbred mice (18 - 20 g) and tetrahybrid CWBA mice (10 - 12 g). Blood samples taken 1, 3, 5, and 7 days following intracranial virus infection demonstrated that CBA/Ca and C3H/A mice produced much more interferon than BALB/c mice and also had a greater mortality rate. The results also showed that the standard Lassa virus strain induces 16 times more interferon production than the remantidine-resistant Lassa virus strain, with mortality rates of 100 percent and 40

percent, respectively. The findings suggest that the correlation between interferon production and mortality rates may be important to the understanding of the pathogenesis of arenavirus infections. Figures 1; tables 2; references 11: 7 Russian, 4 Western.

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### **Antiviral Effectiveness of Ribamidil on Animals Experimentally Infected With Venezuelan Equine Encephalomyelitis**

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[Article by V. A. Markin, Yu. G. Pashanin, V. I. Markov, I. A. Androshchuk, V. A. Pshenichnov, Microbiology Scientific Research Institute, USSR Ministry of Defense, Zagorsk]

[Abstract] Trials of the abnormal nucleoside preparation ribamidil, the Soviet analog to the broad spectrum antiviral drug virazole, were conducted on chinchilla rabbits (2 kg) and guinea pigs (200 g) subcutaneously infected and then administered ribamidil 2 h and 24 h, respectively, after infection, with injections continuing every 12 h until death. Results demonstrated that ribamidil had no protective effect on guinea pigs or rabbits, but it did extend the average lifespan and somewhat reduce virusemia in rabbits. The effectiveness of ribamidil was then tested on baboons (*Cynocephalus*), green monkeys (*Cercopithecus*), and Javan macaques and assessed by its effect on the infection process. The effects of prophylactic/therapeutic administration of ribamidil (100 mg, twice per day, 10 days) included shortening the duration and decreasing the level of virusemia and attenuating the manifestation of some symptoms. Comparative assessment of Venezuelan equine encephalomyelitis among all animals demonstrated that infection in baboons most closely simulates a moderate course of the disease in people. The findings suggest the benefit of ribamidil is possibly due to penetrating the blood-brain barrier in the early phase of the infection process. These observations provide further support for using pathogenetic approaches in laboratory trials on the protective effectiveness of non-specific antiviral preparations. Tables 2; references 7: 2 Russian, 5 Western.

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### **Comparative Description of Some Genetic Traits of Lassa and Mopeia Viruses**

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[Article by N. I. Yerofeyeva, N. M. Trofimov, L. Ye. Surikova, N. S. Vereshchako, F. M. Fidarov, and A. S. Petkevich, Belorussian Epidemiology and Microbiology Scientific Research Institute, Belorussian Soviet Socialist Republic Ministry of Health, Minsk]

[Abstract] A new arenavirus, Mopeia, was isolated in northeast Africa in 1977, where there were no previously recorded cases of Lassa fever. However, it was shown that this new virus was serologically related to the Lassa virus. Because the Mopeia virus is less pathogenic to primates than the Lassa virus, which is very contagious and has a high mortality rate, it is believed that the Mopeia virus may protect the animals from the lethal Lassa virus. Accordingly, a comparative study of some genetic traits of the Lassa and Mopeia viruses was performed to determine whether these traits could serve as criteria of attenuation of the Lassa virus. The results demonstrated that both viruses form plaques on day 6, with the Lassa plaques 2 - 2.5 mm in diameter as opposed to 0.5 - 1 mm for the Mopeia plaques. The thermostability of the viruses was shown to be a poor indicator of virus attenuation. However, the Mopeia virus, like other attenuated viruses, was extremely sensitive to urea, thus demonstrating that urea sensitivity is also a good criterium of change in arenavirus pathogenicity. These findings suggest that the Mopeia virus is an attenuated variant of the Lassa virus, and in connection with data from other studies on the Manchupo and Junin viruses, further demonstrate the urgency of studying the genetic basis of the natural and experimental mutability of viruses in order to produce variants suitable for developing vaccines. Figures 2; references 14: 7 Russian, 7 Western.

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### **Agglutination Test With Soviet Latex Employed to Detect Human Immunodeficiency Virus Antigen and Antibodies to It**

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[Article by S. S. Marennikova, F. S. Noskov, E. M. Shelukhina, E. V. Chekunova, M. V. Polosatov, V. I. Konovalov, G. R. Matsevich, and F. G. Nagiyeva, Viral Preparations Scientific Research Institute, USSR Academy of Medical Sciences, Moscow; Epidemiology and Microbiology Institute imeni Pasteur, Leningrad]

[Abstract] The latex agglutination test (LAT) is similar to the indirect hemagglutination reaction, with the difference being that latex particles are used instead of erythrocytes as the antibody and antigen carriers. Moreover, LAT has the advantages of rapid response and ease of use. Accordingly, a study was conducted to determine whether LAT could be used in the development of a rapid AIDS and HIV diagnostic test. A number of chemical and physical modifications to the polystyrene latex particles were made to determine which would yield the best results. Several factors were shown to affect the quality of production and evaluation of the latex diagnosticum. The results indicated that the only "working" preparation consisted of latex particles with zinc methacrylate 0.6 μm in size in a 1 percent latex suspension. In addition, the maximum titer of antigen detected in the virus-containing materials was obtained from 325 μg immunoglobulin/ml loaded into the latex particles. These findings suggest that a latex diagnosticum using LAT can be produced for detecting HIV antigens. It can

be used in its present form as an auxiliary method for rapid antigen identification in laboratory and commercial HIV cultures. In addition, this diagnosticum can also be employed for detecting HIV antibodies, but it must be further improved. Tables 2; references 16: 4 Russian, 12 Western.

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**Comparative Evaluation of Rift Valley Fever Virus Detection Methods**

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[Article by V. P. Nikolayev and V. A. Tsarkova, Military Medicine Scientific Research Institute, USSR Ministry of Defense, Leningrad]

[Abstract] In view of the fact that the Rift Valley fever virus has been spreading from the African continent towards the southern border of the USSR in recent years, with the imminent danger of appearing in the central Asian republics, a study was undertaken to evaluate various Rift Valley fever virus detection methods. Entebbe and 8-87 Rift Valley fever virus strains were used in cell cultures VNK-21, LLC-MK<sub>2</sub> and Vero, newborn albino mice, antibody fluorescence technique, and indirect hemagglutination reaction. The results demonstrated that it was best to employ cell cultures sensitive to Rift Valley fever virus, which in conjunction with antibody fluorescence technique, can detect minimal concentrations of the virus. Tables 1; references 7: 5 Russian, 2 Western.

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